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Investigating the Effects of Blood Flow on Muscle Fatigue and Recovery in the First Dorsal Interosseous Muscle

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Abstract

The purpose of this study was to gain insight into the physiological principles driving blood flow and fatigue both during and following different levels of intermittent exertion. Utilizing diffuse correlation spectroscopy (DCS) allowed microvascular blood flow (BF) to be observed continuously, providing new insight into the behaviors of BF within the exerting muscle. This experiment was conducted with 11 healthy, adult participants, (5 male, 6 female), fatiguing the First Dorsal Interosseous (FDI) muscle through the abduction of the index finger. The study monitored BF and fatigue in response to 3 levels of intermittent exertion (20%, 30%, and 40% MVC) under constant duty cycle (DC=50%) and cycle time (CT=90s). MANOVA on BF and MVC showed that time, exertion level (EL), and their interaction were significant during both exertion and rest ($p<0.0007$). On average, BF during exertion and rest increased over time and over fatigue, with exertion and resting BF values averaging 1.2 and 3.0 times the baseline, respectively. Differences between exerting and resting BF also increased over time for every EL ($p<0.04$), ranging from about zero to 11 times the baseline BF. At the same levels of muscle capacity (%MVC), resting BF was found to increase with EL consistently ($p<0.05$ for 75, 80, 85, 90, & 100% MVC). Over the 20-minute rest following each session, BF at the same levels of fatigue was also found to increase with EL significantly, but only for the first few minutes of rest ($p< 0.05$); beyond 10 minutes of rest, this positive correlation between EL and rBF independent of MVC was no longer consistent. These findings indicate that during intermittent rest periods, blood flow and fatigue are correlated and increase together, however, EL independently increases BF. This finding is likely the effect of the reflexive BF response, which is correlated to the intensity of exertion (EL). Results indicate that the impact of the reflexive response may be a function of both EL and time, as the differences in BF by EL diminish over extended periods of rest. These findings suggest the presence of a history-dependent recovery rate which is most variable immediately following muscle contraction. Outcomes of this study provide insight into the relationship between BF and muscle fatigue during intermittent exertion, which can be used to provide a physiological foundation for further improvements to models of localized muscle fatigue.

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1. Significance of Muscle Fatigue and Recovery

1.1. Localized Muscle Fatigue (LMF)

Localized muscle fatigue (LMF) is defined as, ‘‘any exercise-induced reduction in force or power regardless of whether the task can be sustained or not’’ (Bigland-Ritchie & Woods, 1984). Independence from task failure is explicitly mentioned in this definition because fatigue is often closely associated with endurance time (ET), or task failure. This creates a perception that fatigue begins at the point of reduced ability to perform a task. In fact, fatigue affects the body upon the initiation of exercise, before the ability to perform a particular task may be reduced (Enoka & Duchateau, 2008). Furthermore, many neuromuscular systems, such as energy reserves, ion concentrations, and the arrangement of contractile proteins, are altered at the onset of exercise (Boyas & Guevel, 2010). Though many parts of the body respond to exercise, LMF is distinctly defined as the reduction of force in the muscle. This differs from whole-body fatigue, which is the result of metabolic demand overworking the cardiovascular system (Chaffin, 1973). Whole-body fatigue occurs at the system level, where multiple muscles are involved, while LMF is evaluated within a single muscle.

LMF is the result of a variety of physiological changes in the body. LMF, then, is expressed through a wide variety of symptoms, including reduced strength, discomfort, decreased coordination, muscle tremor, increased perceived exertion, and altered electromyographic signals (EMG) (Rashedi & Nussbaum, 2015). LMF is of interest because its associated negative effects reduce the ability of a person to perform a task comfortably. Pain and discomfort are the LMF effects that can limit the ability to perform a task or cause task method and form to change over time. However, reduced coordination can affect performance as well. Over a long period, these effects also have the potential to heighten the risk of work-related musculoskeletal disorder (WMSD) (Mair et al, 1996).

1.2. Importance of Fatigue

1.2.1. LMF and Performance

One reason why LMF is an important area of research is the relationship between the symptoms of fatigue and task performance. Some of the symptoms of fatigue include reduced force output, discomfort, decreased coordination, muscle tremor, and increased perceived exertion (Rashedi, 2010). Symptoms like reduced force and discomfort limit ability to complete a strength task comfortably, or at all. Most fatigue studies focus on the connection between fatigue and reduced strength as this feature is embedded into the definition of fatigue: "decrease in maximal force or power production in response to contractile activity" (Wan et al, 2017). Beyond mere strength, however, fatigue can alter muscle timing and muscle coordination, impeding performance, especially for repetitive tasks (Gates & Dingwell, 2008). Muscle tremor is one symptom that heavily affects muscle timing and accuracy. Poor joint stability resulting from fatigue has also been found to affect posture and balance (Davidson & Madigan, 2004; Springer & Pincivero, 2009).

To counteract the negative effects of fatigue on strength and accuracy performance, the body adapts to fatigue by relying on different muscle groups to complete a given task. However, a study in the effects of fatigue on the coordination of multi-jointed movement found that even with natural body adjustments, fatigue causes rigidity in motion and overcorrection in movement (Foresteir & Nougier, 1998). One study in the effects of fatigue found that subjects altered their biomechanical movement patterns in response to muscle fatigue. Though subjects did so in a way that specifically preserved the most relevant features of task performance, performance during fatigue was still reduced from maximum possible performance (Gates & Dingwell, 2008). Any reduction in performance is of concern because it can affect both productivity and comfort.

1.2.2. LMF and Work-Related Musculoskeletal Disorder (WMSD)

In addition to discomfort or productivity concerns, severe LMF has been linked to an increased risk of injury, especially involving muscle strain (Dugan & Frontera, 2000). Risk of injury is important because of its effect on the performance and well-being of the individual, and because of the monetary cost of decreased productivity and medical treatment.

Musculoskeletal disorders (MSDs) are “injuries or disorders of the muscles, nerves, tendons, joints, cartilage, and spinal discs” (CDC, Feb 2018). Work-related MSDs (WMSDs) are cases where these disorders can be either directly related to, or worsened by, the environment and conditions of work. WMSDs are a particularly important category of injury in ergonomics, as the role of the ergonomist is to improve all controllable aspects of the work environment to maximize productivity and safety. According to OSHA, correctly fitting a job to the person helps lessen muscle fatigue, increase productivity, and reduce the number and severity of WMSDs (OSHA, 2019).

It is not clear that LMF causes WMSD. However, for both high exertion level injuries and repetitive strain injuries (RSIs), studies have found that the effects of LMF can make the body more susceptible to WMSD. One study found that fatigue is an important factor in the development of acute muscle strains, as fatigue decreases the ability of the muscle to absorb energy before reaching the degree of stretch that causes injury (Mair et al, 1996). Studies in lower extremity kinematics and kinetics of the single-leg jump, found that fatigue caused a deterioration from neutral to nonneutral alignment, increasing joint loads and resulting in tendon and muscle injury (Liederbach, 2013). This is in agreement with earlier studies finding fatigue leads to decreased joint stability and changes in the biomechanical method of completing a task (Davidson & Madigan, 2004, Gates & Dingwell, 2008). LMF has also been found to be a precursor to RSIs (Valencia, 1986). RSIs, often clinically referred to as “overuse injuries”, are associated with repetitive motion causing pain in ligaments, tendons, and muscles. LMF has been found to occur before RSI and can be used as an indicator of future injury.

In the US in 2017, over 50% of injuries resulting in days away from work were due to sprains, strains, tears, soreness, and pain (U.S Bureau of Labor Statistics, 2017). The high occurrence of injuries which can be linked to LMF makes severe LMF a significant indicator of job safety. It is reasonable, then, to assume that a decrease in the occurrence of high LMF tasks can not only improve the comfort and performance of workers but also have an impact on injury prevention in the workplace.

1.3. Mechanisms of Muscle Fatigue

LMF is a phenomenon that occurs through complex processes and can result from a variety of sources. To understand the sources of fatigue, the pathway of the muscle activation process must be analyzed. LMF takes place at the lowest level in the motor unit (MU). Each MU consists of one motoneuron and all of the muscle fibers it controls. In voluntary contraction, activation of an MU is defined by two sequential processes: the central process and peripheral process.

The central process takes place in the central nervous system (CNS). The central process begins in the primary motor cortex. The upper motoneurons in the cortex propagate a signal to lower motoneurons in the spine (Allen et al, 2008). The peripheral process begins when the axon of the lower motor neuron carries the received signal out of the spine and to the neuromuscular junction (NMJ). At the NMJ, depolarization of the muscle fiber membrane (sarcolemma) triggers an action potential. Then excitation-contraction coupling converts the action potential into a mechanical response (Allen et al, 2008; Boyas & Guevel, 2010; Boundless: General Biology, 2019).

Fatigue can potentially arise at any point in this pathway. Fatigue of the central process is denoted “central fatigue”, while fatigue of the peripheral process is known as “peripheral fatigue”. Central fatigue can be defined as an exercise-induced degradation of the muscle voluntary action (Gandevia et al, 1995). Central fatigue refers to poor motivation, altered central nervous system transmission, or altered recruitment (Kirkendall, 1990). Some of the physiological causes of central fatigue include the blocking of action potentials at axonal branching sites, drops in motoneuron discharge rate due to stimulation of types III and IV nerves, and reduced excitability of the cells within the motor cortex (Ament & Verkerke, 2009). Electrical stimulation to the muscle can be used to indicate the presence of central fatigue, as the result of an electrical stimulus to the muscle is equal to the maximum voluntary contraction (MVC) if the effect of central fatigue were not present (Merton P, 1954).

Peripheral fatigue takes place in the processes after axon travel to the NMJ commences. Peripheral fatigue has many causes, most of which can be attributed to alterations in excitation or alterations in cell metabolism (Fitts, 1994). Fatigue in the peripheral system depends heavily on the strength and duration of contraction. For high-intensity exercise, disturbances in E-C coupling and inhibition in sarcoplasmic Ca^{2+} release are more likely to occur. This is because ATP, the energy of the cell, can be produced aerobically or anaerobically through glycolysis, or from small ATP reserves through lipolysis (MacIntosh et al, 2012). During high-intensity exercise, an O2 deficit is created because the acceleration of glycolysis is faster than that of the oxidative pathway (Sarelius & Pohl, 2010). Lack of O2 results in the anaerobic creation of ATP. This creates a buildup of inorganic phosphate (Pi), H^+ ions, and lactic acid along with ATP (Green, 1997). The concentration of these metabolites have direct effects on the efficiency of cross-bridge interactions and inhibit peak force (Ament & Verkerke, 2009). When contraction intensity is below the point of onset of blood lactate accumulation, ATP can be created aerobically, and the depletion of muscle glycogen contributes to peripheral fatigue (Fitts, 1994).

1.4. Mechanisms of Muscle Recovery

1.4.1. Blood Flow and Oxygenation

Blood flow is critical in sustaining and recovering the muscle contraction process as it brings oxygen necessary for aerobic ATP production, and removes by-products of metabolic processes (Wan et al, 2017). A close relationship is known to exist between the supply of oxygen to the muscle, and the somatic neural recruitment of motor units (Thomas & Segal, 2004). In an experiment concerning fatigue in the triceps brachii muscle, initial force output decreased during MVC (Martin et al, 2006). When blood flow was occluded, the decreased force output remained depressed even after a period of rest. Once blood flow was returned to the muscle, however, the initial force was restored within 15s. Another experiment to compare recovery when blood flow was normal versus occluded, was conducted in the biceps brachii (Bigland-Ritchie et al, 1986a). Similarly, this experiment found over 3 minutes of rest, the muscle did not recover while occluded. However, the same amount of time produced complete recovery when blood flow was kept at a normal level. Not only does occlusion prevent recovery following exercise, but a study using a handgrip exercise also suggests that occlusion exacerbates fatigue development both during and after exercise (Broxterman et al, 2015). Though occlusion affected both central and peripheral fatigue, peripheral fatigue was found to be significantly more sensitive to occlusion. Blood flow is not only important but necessary for oxygen delivery and fatigue recovery.

Deoxygenation of blood occurs at rest at an extraction rate of between 20 and 40% of the total oxygen reserves in the blood (Van Beekvelt et al., 2001). Some work in near-infrared spectroscopy (NIRS) has shown that, overall, the body prefers to vasodilate and introduce more blood flow, rather than draw from blood oxygen reserves at an increased rate (Joyner & Casey, 2015). This likely because increased oxygen extraction from the blood creates an increase in local pCO_2 and H^+ concentrations (Sarelius & Pohl, 2010). Therefore, when possible, the muscle will receive all oxygen replenishment from a simple increase in blood flow. As the difficulty of exercise increases, however, increased blood flow alone cannot replenish metabolites. This is because, simultaneously, the sympathetic nervous system—part of the body's autonomic system—is working to maintain healthy arterial blood pressure (Thomas & Segal, 2004). The simultaneous maintenance of healthy blood pressure and a constant deoxygenation rate compete as the difficulty of exertion increases. When a continuous increase in blood flow exceeds healthy blood pressure, the sympathetic nervous system wins over and will stop the increase of the flow. The tissue will then compensate and extract oxygen at a lower rate, as high as 70-80% of the optimal level during heavy exercise (Korthuis, 2011).

At levels of exertion associated with aerobic ATP production, (specific to an individual muscle's capacity), deoxygenation rate is stable (Joyner & Casey, 2015). This creates a direct correlation between blood flow rate and oxygenation level. However, since rates of deoxygenation can change at the onset of exercise, or when exertion level is high, this correlation can become complicated. However, it remains that blood flow is the first and primary response to exercise, and, thus, is a relevant indicator of recovery for submaximal occupational exertions.

1.4.2. Vasodilation

The vasodilation that occurs to satisfy the requirements of muscle contraction and prevent high rates of deoxygenation can occur whether actively exerting force or at rest. The classic metabolic signals initiating vasodilation include K^+, Adenosine, CO_2, and H^-/Lactate—all of which are produced during exercise (Sarelius & Pohl, 2010). During exercise, the somatic nervous system senses the voluntary activation of skeletal muscle through these metabolic indicators and, as a result, vasodilation and functional hyperemia occur. The specific contribution of each of these metabolites in mediating hyperemia is unknown. Vasodilation has been found to occur at the onset of exercise, within 5s of the exerting muscle. Because the metabolic vasodilator system works more slowly than observed vasodilation responses, there is likely another cause of vasodilation that occurs at the onset of any exercise. This is thought to be a reflex response to muscle deformation (Rowell & O'Leary, 1990).

At rest, skeletal muscle blood flows may be as low as 1-4 ml/min; maximal vasodilation has been found to increase muscle blood flow to as much as 50-100 ml/min (Klabunde, 2012). While vasodilation physically increases the size of veins and arteries to allow for this increase in blood flow volume, capillaries do not have the smooth muscle required to vasodilate. Instead, capillary blood flow is controlled by pre-capillary sphincters. These sphincters open and close to allow blood to pass through capillary beds. At any given time, only 5-10% of these sphincters are open, so during exercise, the number of utilized capillary beds increases to account for increased blood flow demand. Increased blood flow is managed by blood volume in the capillaries because capillary blood velocity must remain slow to allow for efficient exchange (Molnar & Gair, 2019).

Vasodilation is regulated by metabolic requirements but is ultimately limited by the autonomic system's regulation of blood pressure. Intramuscular pressure can serve as a hindrance to vasodilation; just as externally applied pressure results in occlusion (as with a blood pressure cuff), the internal pressure caused by muscle activation can also occlude blood flow. Though the response to muscle activation is to increase the blood supply to the muscle, this relationship is complicated by the mechanical hindrance of muscle contraction (Bangsbo & Hellsten, 1998).

Rate of recovery, then, is related to some function of both intramuscular pressure and level of muscle activation and resulting metabolic deficits. Though the relationship between blood flow and fatigue rate has been discussed, few definitive conclusions have been drawn from blood flow measurements before the recent development of non-invasive measurement systems of blood flow and oxygenation (Kumar, 2006).

1.5. Assessing Blood Flow

A variety of blood flow measurement technologies are currently being used. Among these, three techniques in assessing the muscular blood flow are briefly introduced, i.e., Doppler ultrasound, near-infrared spectroscopy, and diffuse correlation spectroscopy.

1.5.1. Doppler Ultrasound

One popular tool is doppler ultrasound, in which a transducer is placed above a blood vessel to send and receive ultrasound waves. These sound waves bounce off blood cells, so any blood movement produces a change in the pitch of received waves. Blood flow, then, produces the Doppler Effect which can provide information on the kinetics of blood flow through the vessel (Healthwise, 2019). Doppler ultrasound is used frequently in vascular studies to test for blood clotting, and in the area of obstetrics to observe blood flow to an unborn baby. In the area of single-muscle fatigue and recovery, however, Doppler ultrasound is difficult to apply. The direct increase in blood flow to a single muscle can only be definitively observed at the capillary level, where ultrasound cannot be used. An artery large enough to measure by ultrasound supplies blood to a host of muscles. Thus, there is no direct way to measure changes in blood flow to a single muscle by measuring blood flow at a major artery. A related technology, perfusion MRI, has been developed to measure blood flow at high spatial resolution in the microvasculature system, however, the high cost and low mobility of the instrument makes its application practically limited to the area of brain scanning. Laser doppler also measures blood flow similarly, but only at the superficial level (~1mm depth), making it inapplicable for deeper muscles (Hou et al., 2019).

1.5.2. Near-Infrared Spectroscopy (NIRS)

To remedy these deficiencies, Near-Infrared Spectroscopy (NIRS) has been developed. Near-infrared light consists of wavelengths between 700 and 1000 nm. This wavelength region is referred to as the "window to living organisms", as these wavelengths easily penetrate living beings (Shimadzu Europa GmbH, 2019). However, as light passes through tissue, some scattering and absorption of light can take place within this region. Scattering accounts for about 80% of light attenuation and absorption accounts for the other 20% of light attenuation (Pellicer & Bravo, 2011).

To separate the effects of scattering and absorption, a continuous intensity instrument can be used, where a change in attenuation is approximately representative of a change in concentration of absorbing compounds (Delpy & Cope, 1997). Major absorbing compounds in biological applications include oxygenated hemoglobin, deoxygenated hemoglobin, melanin, and water. Of these compounds, oxy- and deoxyhemoglobin, are the only compounds that are oxygen-dependent and non-constant in the NIR region (Delpy & Cope, 1997). Because oxy- and deoxyhemoglobin are compounds that are oxygen dependent, this measurement of change in absorbance produces an estimate of the change in oxygenation. Over time, these changes in oxygenation produce an estimate of muscle blood flow (Lucero et al, 2018).

Some have questioned the accuracy of NIRS measurements, as no correlations between blood oxygenation level, or blood volume and fatigue have been found using this method (Kumar, 2006). Most of the studies using NIRS, however, focus on the quadriceps or forearm where muscles measured are relatively dense and large. One quadricep study suggested that NIRS may not measure deep enough into the muscle (Schlup et al, 2015). This is supported by healthcare application, which has proven NIRS reliable for "up to several centimeters" of measurement—possibly too small of a range to penetrate a large muscle (Hou et al., 2019). Additionally, there are certain limitations of applying NIRS to peripheral oxygenation measurements which can complicate results. Hemoglobin and myoglobin have similar optical properties. When applied to cerebral oxygenation measurement, or breast tissue measurement, where muscle and myoglobin are minimal, NIRS is reliable. However, when addressing peripheral oxygenation, such as in the quadricep or forearm, myoglobin may be mistaken for hemoglobin, and hemoglobin saturation can be overestimated (Scheeren et al., 2012). Relative changes in hemoglobin and myoglobin oxygenation need to be quantified to separate the effect of oxygen delivery from oxygen utilization. Pulmonary VO_2 kinetics can be used to represent oxygen utilization during exercise, but VO_2 measurements are valid only for relatively steady-state conditions (Spires et al., 2011). Thus, NIRS, even when combined with VO_2 may be limited in peripheral muscle analysis, especially where the muscle is large or dense.

1.5.3. Diffuse Correlation Spectroscopy (DCS)

Diffuse correlation spectroscopy (DCS) is a dynamic form of NIRS technology, which has been rapidly developing. Using a long-coherence length laser, single-mode fibers, a single-photon-counting avalanche photodiode (APD) detector, and an autocorrelator board, DCS quantifies the speckle fluctuation of diffuse light through tissue. Fluctuations are sensitive to the motion of red blood cells within microvasculature, thus permitting fast assessment of blood flow in deep tissues (Hou et al., 2019). Rather than implying blood flow from oxygenation measurements, DCS can collect information on how photons are dynamically scattered using single-mode fiber. A blood flow index (BFI) can then be fit which depends directly on the motion of red blood cells. DCS has been implemented extensively in the area of cerebral blood flow, and has been validated using laser doppler, doppler ultrasound, arterial-spin labeled MRI, and against both invasive and non-invasive measures of tissue physiology (Durduran et al., 2010). DCS has also been applied to measure blood flow in the skin, muscle, breast, and other tissues. Applications of DCS to peripheral muscle have continued to expand: an algorithm has recently been created to remove motion artifacts from DCS measurements to improve the accuracy of measurement in dynamic exercise (Quaresima et al., 2019).

DCS can be relevant in developing a clear understanding of fatigue at the motor unit level. Microvasculature is where muscle fibers receive metabolic replenishment, so, to apply accurate measurements of blood flow to models, the observation of blood flow at the capillary level is fundamental to understanding the true recovery process. Until recently, the methods for measuring blood flow in microvasculature were limited to inferences based on NIRS, and results were inconclusive. DCS provides a new method for more direct measurement of the blood flow in microvasculature.

2. Muscle Fatigue and Recovery Modeling

2.1. Modeling Methods

Due to the complexity in the chain of the force production process, and subsequently, muscle fatigue, the modeling methods and parameters in localized muscle fatigue (LMF) modeling vary substantially (Enoka, 1995). The prediction of LMF by modeling is important to fitting a task to the capabilities of the worker population and maximizing worker performance and safety. Each model is created under different assumptions, can be applied to different types of tasks, and is applied with a different level of accuracy. Among these varying models, however, there are three general modeling approaches: experimental data-driven regression modeling, theoretical, physiology-based modeling, and theoretical, phenomenal parameter-based modeling (Xia, 2014).

2.1.1. Empirical Modeling

Data-driven regression modeling is often used to predict a point of task failure, or endurance time (ET). Data-driven regression modeling is also referred to as empirical modeling; these models vary controllable task parameters and fit the model to observed results (Rashedi, 2016). The simplest of these models investigate prolonged static exertions and have found a curvilinear relationship between exertion level (EL) and ET (Rohmert, 1960). Models of intermittent static exertions have found cycle time (CT) and duty cycle (DC) to be additional significant factors in predicting ET (Kahn & Monod, 1989, Iridiastadi & Nussbaum, 2006). Through empirical studies, it has been found that both task attributes and personal factors are significant in predicting fatigue progression (Ma et al, 2013).

A principal advantage of empirical models is the ability to modify them for a specific situation (Rashedi & Nussbaum, 2015). For example, an empirical job rotation model using integer programming was applied to meet safety criteria and minimize job severity index for a series of lifting tasks (Carnahan et al., 2000). ET models have been developed for numerous muscle groups in static conditions (El Ahrache et al, 2006). One model combined ET single-muscle models to create a complete dynamic biomechanical model of the forearm with the capability to estimate fatigue and muscle capacity (Fruend & Takala, 2001). For these and similar applications, empirical modeling results in accurate and directly applicable outcomes.

One disadvantage of empirical modeling is its lack of generalizability. General principles of fatigue cannot be definitively concluded from empirical data, and models can often only be accurately applied to the situation the experiment explicitly tested. For example, a 2014 model in forearm and calf submaximal contractions found that fatigue does not fit a simple linear model, but may be better fit by multi-phase linear models (Green et al, 2014). The statistical work was extensive, and the results informative concerning the principles of fatigue. However, the results are not robust to changes in muscle phenotype, sex, age, or clinical status. The inability to extrapolate data fundamentally exists within all empirical models. A recent exponential model for fatigue tends to overestimate ET for low ELs, and underestimate ET for high ELs, as the function exhibits nearly asymptotic tendencies around 0% MVC and 100% MVC (Frey Law & Avin, 2010). The inflexibility of empirical model application also limits ET model prediction to static tasks, as the models cannot account for recovery or changes in physical capacity (Rashedi & Nussbaum, 2015).

2.1.2. Theoretical Modeling

Theoretical modeling aims to take the principles observed through empirical modeling and create more generally applicable models. Physiology-based models are generally complex with a variety of parameters. These models are based on the physiology of force generation. In these theoretical models, there is a distinct focus on the relationship between metabolic state and fatigue. One model includes Ca2+ concentration as a major indicator of fatigue level (Ding et al., 2000). Another model relates anaerobic ATP creation to fatigue and inputs metabolic factors such as muscle pH and H^+ concentration as an indicator of fatigue (Noakes, 2000). These models strive to model fatigue at the most fundamental level and focus on quantitative physiological measurements. Theoretical, parameter-based modeling is also based on physiology but takes a systems approach to understand fatigue development. These models often focus on the motor unit (MU) as the building block of the fatigue process. ODE models have been developed to explain the relationship between task parameters and fatigue at a systems level, some separating fatigue and recovery into two different equations and processes (Freund & Takala, 2001; Ma et al, 2009). On the other hand, a series of models have been developed based on defining states for the pool of motor units (i.e., three compartments) (Liu et al, 2002; Xia & Frey Law, 2008; Xia, 2014). In this approach, MUs exist in one of the three states of fatigued, active, or at rest. The rate that MUs move between each state is determined by a combination of task parameters and individually fit fatigue and recovery rates (Liu et al, 2002). In a more recent effort, different types of muscle fibers are considered, and the activation of different types of MUs based on exertion type is found to create different results (Potvin & Fuglevand, 2017).

The main advantage of physiological and parameter-based modeling is that once validated, these models have the potential to make fatigue and recovery modeling widely applicable, quantitative, and based on measurable and validated inputs. Existing theoretical models have been useful in clinical applications where electrical stimulation is used to activate the muscle, as this method negates the effect of central fatigue and simplifies the purpose of application (Binder-Macleod & Snyder-Mackler, 1993). To further reduce complexity, theoretical models often focus on maximal contraction (Xia, 2014). The maximal contraction case eliminates any variation that results from the recovery that can take place at low levels of exertion, allows for easy normalization of EL between individuals, and allows for faster evaluations of endurance time. However, there is still room for theoretical modeling to continue to expand into the area of submaximal voluntary contraction.

The disadvantage of theoretical models is the modeling complexity and the invasive and time-consuming nature of metabolic measurement. Some physiological models include up to 30 parameters (Giat et al., 1993). To avoid intensive measures, recent models measure metabolic processes using spectroscopy. CrP, Pi, and pH are measured using phosphorous magnetic resonance spectroscopy (P MRS), and blood flow measurement is taken using Near-infrared spectroscopy (NIRS) (Baker et al., 2010). These methods, though available, are relatively new and expensive, and so are not present in many studies of fatigue (Kumar, 2006). Parameter-based theoretical models use a systems approach to avoid some of the complexity of pure physiological models while retaining a foundation in valid physiological processes. However, these models still face the difficulty of modeling and validating a highly complex process with a simple robust method.

2.2. Analysis of Relevant Models

A foundation in physiological sources of fatigue and the potential of wide application has led many to develop the area of theoretical modeling. Theoretical modeling is the best way to combat model complexity, increase computational efficiency, and point models toward occupational relevance.

Following a study in occupationally relevant models in 2015, four of the most relevant theoretical models of fatigue were found to be MU-based theoretical models: Liu's three-compartment model, Xia and Law's model, Ma's ODE model, and Potvin's MU type model (Ma et al, 2009, 2010, 2011; Xia & Frey Law, 2008; Liu et al., 2002, Potvin & Fuglevand, 2017). These models are advantageous, as they are computationally efficient and rely upon physiological processes to ensure generalizability. These models all use parameter-based theoretical modeling and focus on the fatigue state of MUs in a single muscle.

2.2.1. Liu's Three-Compartment Model

The purpose of introducing a three-compartment model was to better reflect physiological processes and involve the CNS in modeling LMF development (Liu et al., 2002). Each compartment of the model represents an MU state—that is, active (M_A), fatigued (M_F), or at rest (M_{UC}). The model contains four foundational parameters to account for individual differences: a fatigue factor (F), a recovery factor (R), a brain effort variable (B), and the total number of MUs in a muscle. F, R, and B are fit parameters found through experimental data fitting. The way that MUs move between compartments is driven by F, R, and B fits and two ODEs. One ODE explains the change in the number of fatigued MUs, the other explains the change in the number of active MUs. The rate of change between rest state and active state is determined by constant, B.

When compared to experimental data, the shape of the theoretical curve closely matches experimental data, implying accurate assumptions and a good representation of fatigue and recovery in the muscle. The approach and logic of the model are innovative and were validated under conditions of constant, maximal effort (Liu et al., 2002). However, it is largely simplified to validate the approach. Fatigue and recovery processes are assumed to be mutually exclusive, F and R are constant, and B is set to its maximum value (Ma et al., 2009). These simplified conditions limit this initial model to maximal static exertion.

2.2.2. Xia & Frey Law's Adaptation of the Three-Compartment Model

Xia & Frey Law built upon Liu's model so that it can be applied at submaximal and dynamic conditions (Xia & Frey Law, 2008). Rather than explaining the movement between active and rest states using B, a new variable C(t) is introduced. In Liu's model, transfer with a constant B was wholly dependent on M_R and M_A compartment sizes; here, C(t) controls activation and deactivation patterns and is dependent on both task demand and MU availability. Within C(t), two more fit parameters become necessary—force development rate (L_D) and relaxation rate (L_R). The model is fairly robust to changes in L_D and L_R, as the time course of these variables is negligible compared to the time course of fatigue development. Thus, these parameters are set arbitrarily to a value.

Through these innovations, the model can be applied to submaximal and dynamic exercise conditions. However, the application of the Xia & Frey- Law model is still limited—especially in the area of predicting low-medium submaximal, intermittent contraction (Rashedi & Nussbaum, 2015). One source of this model limitation is the constant R parameter. The constant F parameter can be considered reasonable, as it is based on the excitation-contraction event which takes place uniformly within the muscle fiber; the constant R, however, is based on the replacement of oxygen and glucose by the bloodstream and is necessarily dependent on occlusion during contraction (Xia, 2014). Though the model fits sustained contraction well, (excluding ~0 ELs), recovery during sustained exertions is very different from recovery during intermittent exertion. The fit R parameter can change by as much as 700% when being fit to intermittent versus sustained work (Rashedi, 2016).

Further work introduced a variable recovery rate, based on a linear relationship between blood flow and recovery, with occlusion determined by the level of exertion (Xia, 2014). This model, however, resulted in a significant under-estimation error, and, at best, produced equivalent results when compared to the constant R model. This is likely due to some oversimplified representation of the relationship between blood flow and occlusion. Looft introduced a recovery that differentiates between complete rest and rest during exertion (Looft, 2014). The multiplier was successful in improving predictions of fatigue during periods of intermittent contraction but resulted in a large error when predicting ET.

2.2.3. Miura, Nishida, & Shirase's adaptation of the three-compartment model

Miura et al. carried on the work of Liu, Xia, and Frey Law to improve and further adapt the three-compartment model (Miura et al., 2019). In Miura's model, they aim to address poor recovery modeling and poor prediction at low EL. This improvement to the model was facilitated by differentiating between slow and fast-twitch fibers. Considering the difference in fatiguability between fast and slow twitch muscle, this integration was physiologically grounded. The model worked well for static, ET work. However, when the model was fit to intermittent work, results were slightly underestimated.

To account for this underestimation, a new definition of recovery is defined. Recovery is a function of both slow and fast-twitch muscle fibers and the amount of currently active motor units. This more detailed idea of recovery provided a more accurate prediction of EL during a maximal, intermittent task. The model was only validated under conditions of maximal, intermittent exertion, and results were only collected for one participant. Though the model considers changes in fast twitch and slow twitch muscle fiber contributions under submaximal conditions, these conditions are yet to be tested and compared to model predictions. Results, though improved, also lack statistical power as they are derived from a population of one.

2.2.4. Ma's Simple ODE

Ma's model, compared to the three-compartment model, results in similar fatigue predictions for sustained exertions. However, there are some deviations in model predictions during intermittent contraction (Rashedi & Nussbaum, 2015). Though the model relies on Liu's MU state logic, Ma's model uses a slightly different approach. This MFM contains two independent ODEs for fatigue and recovery and relies on fit parameters F and R. MU recruitment type patterns and individual factors are considered implicitly in this model.

Similar to Liu or Xia & Frey Law's models, Ma's model also shows high sensitivity to the changes in the model parameters at low EL, and inaccuracy in predicting fatigue during dynamic conditions (Rashedi, 2016). They introduced separate models for fatigue and recovery processes, which is not necessarily reflecting the actual process in the human body, where we have simultaneous fatigue and recovery processes. Meanwhile, during maximal exertion, where occlusion is high and relatively consistent, a separate and constant recovery process results in good estimates during the rest period subsequent to muscle exertion. However, when recovery during exertion is emphasized, as in low ELs or intermittent work, the recovery model is not applicable to help with the muscle capacity prediction.

3. Relevant Blood Flow and Fatigue Studies

Though parameter-based models have been found to be logically sound in modeling fatigue, there remains a need to develop a more physiologically representative model of recovery (Rashedi & Nussbaum, 2017). Even in the most promising motor unit (MU) models, recovery has been represented implicitly, rather than physiologically. Though variations to the three-compartment model are continuously made, these are often limited to static exertion and/or maximal exertions. More recent recovery modeling improvements from Xia, Looft, or Miura have begun to allow for intermittent exertion models (Xia, 2014; Looft, 2014; Miura et al., 2019). Xia provided a varying recovery parameter based on exertion level; Looft added a recovery parameter to account for changes during total rest; Miura implemented a recovery parameter based on fast and slow twitch muscle fiber recruitment percentages to account for intermittent rest. To make modeling more relevant to dynamic conditions, however, a foundation of physiological understanding of blood flow (BF) during dynamic exercise must be established. An informed understanding of recovery is necessary.

The investigation of recovery parameters like blood flow and blood oxygenation is not new to the field of fatigue, however, it has not been directly applied to a theoretical, occupationally relevant model. In existing investigations of blood flow during exercise, many experiments consider the effect of total or partial occlusion (Pitcher & Miles, 1997; Cole & Brown, 2000; Wernbom et al., 2006; Broxterman, 2015). These studies rely on blood flow measurements to the entire extremity. Other partial occlusion experiments have also been performed which rely on other types of blood flow measurement, but are limited in accuracy and application by blood flow measurement technologies (Wigmore et al., 2004; Ferrari et al., 2011; Taelman et al., 2011).

3.1. Application-limited studies in blood flow during exercise

Numerous studies investigate the effects of total BF occlusion during exercise (Pitcher & Miles, 1997; Cole & Brown, 2000; Wernbom et al., 2006; Broxterman, 2015). The consensus among these studies states that occlusion adversely affects recovery and fatigue development. Wernbom et al, among others, have found that as exertion level increases, blood flow measurements approach the occluded control measurement, which implies blood flow changes based on exertion level. Further, this implies that the natural occlusion that takes place in the muscle may affect blood flow similarly to external venous occlusion. These studies provide critical information, but this form of blood flow quantification relies on venous occlusion at the limb. This limits the application of this information, as blood flow measurement at the artery is not directly correlated to blood flow measurement in the microvasculature of a single muscle (Schlup et al., 2015). Additionally, when using venous occlusion plethysmography, measurements can only be made following exercise, so these studies provide no data for how blood flow may change during contraction.

3.2. Technology-limited studies in blood flow during exercise

3.2.1. Perfusion MRI

Experimental results regarding partial occlusion are often complicated due to the difficulties in obtaining a valuable and non-invasive measure of blood flow to a specific muscle. One existing study using perfusion MRI (pMRI) is one of the few applications of pMRI to skeletal muscle. This study enabled the measurement of blood flow during contraction, and the results demonstrated that blood flow is proportional to the exertion level (Wigmore et al., 2004). This study found that occlusion linearly increased with MVC, and complete occlusion occurred around 60% MVC. These findings agreed with venous occlusion results, but only four subjects were used to compare the methods, decreasing statistical power. The method also contained a high level of error. The authors reported numerous sources for error in the signal intensity measurement, and results contained large motion artifacts. There was also a significant concern for whether all capillaries could be seen, due to their varying orientations and the limited resolution of the system. Though the patterns of blood flow response can be seen, quantification and conclusions were difficult to verify under a data set of eight and significant errors.

3.2.2. Near-Infrared Spectroscopy

Studies using NIRS have been most promising recently, as they have provided important information regarding blood oxygenation. NIRS has been applied to study muscle damage, ergonomics, heterogeneity of muscle O_2 supply and demand, muscle activation, and respiratory muscle blood flow (Ferrari et al., 2011). Some studies have found oxygenation values to be highly correlated with blood volume in the muscle, making oxygenation a reasonable measure of recovery (Fujimoto et al., 2007). However, there has been little direct application of NIRS to skeletal muscle fatigue.

Two studies that focus on muscle activation and NIRS in the single muscle, look at EMG and NIRS simultaneously, looking for similar patterns between measurements of muscle activity. One study found that though oxygenation was negatively correlated with the time length of isometric contraction; the linearity of correlation, however, was dissimilar to EMG results. In addition, R^2 values for this correlation were low, and some results were found to disagree with past measurements (Taelman et al., 2011). This lack of correlation between EMG and NIRS, suggests that the measurements are distinct and cannot be interchanged. There is a more complicated relationship between EMG and NIRS. A similar study comparing NIRS and EMG found that NIRS measurements were highly affected by outside factors such as motion, which led to inconclusive results (Gersak & Gersak, 2009).

NIRS measurements during muscle activation have not been conclusive regarding the physiology of recovery during or following exercise. One reason is the wide variety of NIRS measurements, technologies, and outputs that have been used in these studies (Hamoaka et al., 2007). This lack of agreement in how signals are obtained and interpreted makes comparing between studies difficult. Other concerns are focused around the repeatability and overall reliability of measurements. There is distinct concern regarding the effect of myoglobin desaturation on the NIRS signal, which is a concern based on the logic of the technology (Scheeren et al., 2012). Another concern that affects many of these studies is the effect of motion, both deformation of the muscle and overall movement, in collected NIRS data during exertion.

Overall, there is a lack of studies directly considering how NIRS measurements can provide insight into muscle recovery. Those studies that do measure NIRS during skeletal muscle activation provide little conclusive quantification of the relationship between fatigue state and blood flow measurement.

4. Research Gaps/Objectives

In empirical fatigue modeling, there are several models for isometric contraction. Among these are a series of models that use a three-compartment approach to characterize fatigue-state at the motor-unit level (Liu, 2002; Xia & Frey Law, 2008; Looft, 2014; Xia, 2014; Miura et al., 2019). The most recent modifications of these models have been aimed at improving the flexibility and accuracy of parameters, to eventually model dynamic conditions, while most recent studies focused on modeling the fatigue and recovery during intermittent contractions.

A recurring focus of these developing models has been the implementation of a variable recovery parameter. Recovery parameters have been introduced which adjust for the condition of total rest, change with exertion level, or change depending on the amount of active fast-twitch fibers (Looft, 2008; Xia, 2014; Miura et al., 2019). Outcomes of the exertion-level dependent model were not substantially different from previous, non-variable recovery models. The total rest multiplier model reported improvements in predicting muscle fatigue during intermittent contraction but produced a substantially larger error in predicted ETs. The fast-twitch fiber dependent model improved prediction during periods of intermittent contraction but was only verified under the simplified exertion level of 100% MVC. The reported errors in prediction and limited application of these models may be due to an over-simplification of the recovery parameter (Rashedi & Nussbaum, 2015). Blood flow is the vehicle for recovery (Thomas & Segal, 2004). Thus, to improve the recovery parameter, blood flow and fatigue must be simultaneously observed and characterized. To make this relationship clear and avoid the complex biomechanical systems, blood flow response must be first observed within a single muscle.

The research gap is in lack of accurate quantification of the patterns and magnitude of muscle blood flow variation during and after contraction within a simple biomechanical system. Though blood flow is known to change under varying conditions of muscle contraction and rest, the quantification of this variation within a single muscle has been complicated by technological challenges. As discussed previously, current measurements of blood flow during exercise are either focused on arterial measurement, cannot be measured during exertion, or contain a high level of error due to technological limitations. Diffuse correlation spectroscopy (DCS) is a newer blood flow measurement method, first appearing in labs before 2000, but extensively validated in humans beginning in 2010 for use in a wide range of clinical applications (Durduran & Yodh, 2014). DCS provides an opportunity to conduct accurate and continuous measurements of blood flow throughout the contraction (Hou et al., 2019). Observing blood flow changes while monitoring fatigue may provide insight into the relationship between muscle recovery and blood flow, serving to provide physiological data to inform future modeling developments.

5. Methodology

Given the need to observe and quantify how blood flow (BF) changed throughout the exertion and over the periods of intermittent rest, an experiment was conducted to analyze the effects of exertion level (EL) on BF and recovery during intermittent fatiguing exercises. The experiment was designed around the abduction of the index finger, as the FDI muscle is the only muscle in charge of this exertion, producing a simple, biomechanical system for analysis.

5.1. Participants

Twelve moderately active, healthy participants with no existing MSDs, (6 female and 6 male), were recruited from the university and the local population. Their mean (SD) age, height, and body weight were 22.2 (1.95) years, 69.2 (3.51) inches, and 154.5 (28.96) pounds, respectively. Aside from being healthy, active, and free of any underlying MSDs, participants were pre-screened for their ability to perform the fatiguing task to standard. Informed consent was collected from participants, as approved by the Rochester Institute of Technology IRB.

5.2. Experimental Procedures

Each subject participated in a preliminary session where experimental procedures were explained, and consent was confirmed. Initial tests of feasibility were conducted to ensure participants could adequately conduct the tracking task required to fatigue the first dorsal interosseous (FDI). Following this screening, each participant conducted three subsequent experimental sessions. Each session involved fatiguing the FDI through controlled index finger abduction at a distinct exertion level. Sessions were separated by a minimum of three days to avoid the effects of long-term fatigue.

The experimental procedures for each experimental condition are presented in Figure 1.

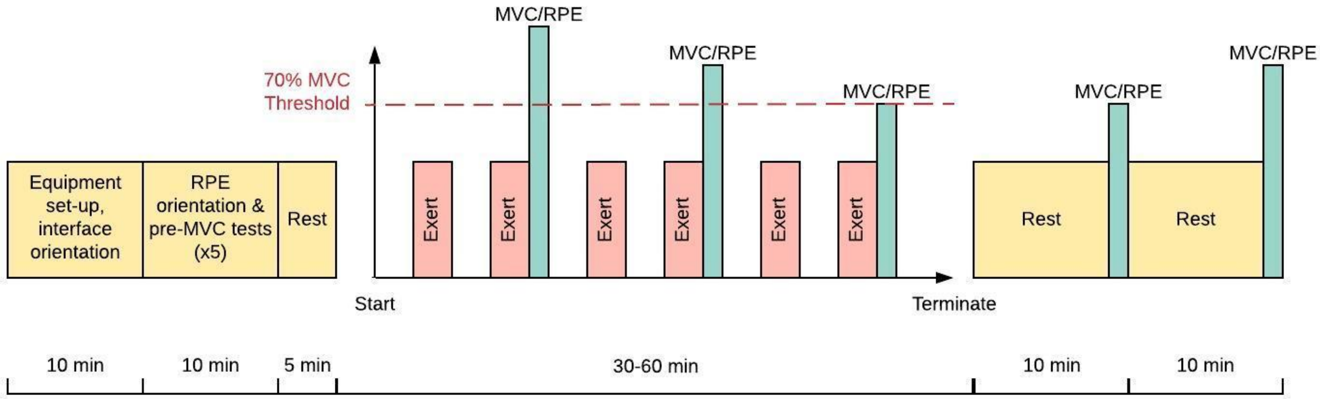

Figure 1: Procedure for one experimental run with an abridged fatigue scenario.

Each participant was introduced to the Borg CR-10 scale during rating of perceived exertion (RPE) orientation. To calibrate their RPE, participants were asked to lean against a wall and bend their knees at a 90-degree angle, as has been conducted in previous studies (Rashedi et al., 2014; Sood et al., 2007; Rashedi & Nussbaum, 2015).

Subjects were then oriented to the experimental equipment and secured in the test fixture. A finger splint was applied to the right index finger to prevent the exerting finger from bending during the experiment and contacting any surface beside the load cell. Participants were asked to sit upright behind the table and face the display screen. Then participants placed their right arm on the table, with forearm pronated and palm flat on the table surface. The arm was bent to 135 degrees with shoulder abducted to maximize FDI isolation, as in previous studies (Rashedi & Nussbaum, 2015). The fixture was adjusted for the individual participant so that the second knuckle of the index finger was secured against the side of the load cell, the diffuse correlation spectroscopy (DCS) probe was over the belly of the FDI, and the arm was comfortably and properly strapped (see figs. 1, 2, & 3).

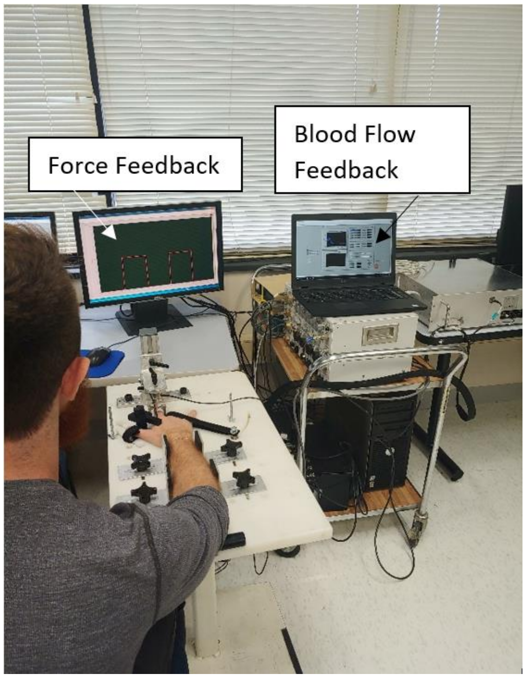

Figure 2: A Participant is seated behind the fixture with the force feedback screen in clear view. The torso is upright, the arm is bent to 135 degrees, and the shoulder is abducted to allow for maximal isolation of the First Dorsal Interosseous (FDI).

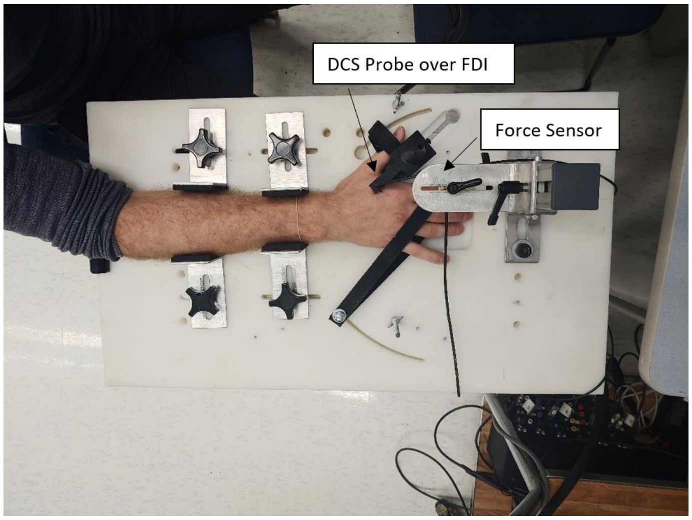

Figure 3: The participant’s arm was fixed by 4 clamps around the lower and upper forearm with a stop was placed behind the elbow. The right index finger was placed in the force sensor, and all other fingers and the thumb were secured in Velcro straps. The diffuse correlation spectroscopy (DCS) probe is placed over the belly of the First Dorsal Interosseous (FDI).

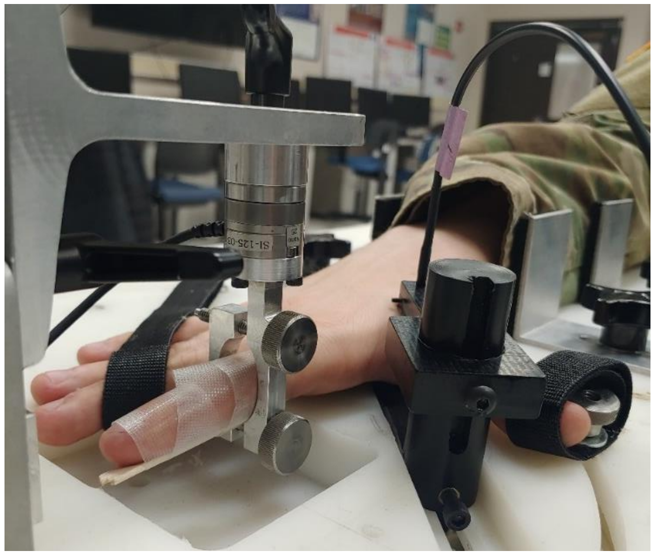

Figure 4: A participant's hand is secured in the fixture, as in Fig. 3. The splint has been applied to the right index finder to avoid bending of the finger throughout the session. The second knuckle of the index finger is aligned with the edge of the load cell for force application in index finger abduction.

Once secured, the maximum voluntary contraction (MVC) trial consisted of 3-4 repetitions of 3-5 second bouts of maximal index finger abduction force. During the trials, the participant was verbally encouraged to perform to the best of their ability while retaining the body posture described above. Maximal values found through these trials were used to calculate the exertion levels for the following fatiguing exercise.

Following a rest period (~5 minutes), participants completed the working period including the intermittent exertions (see Figs. 5, 6, and 7). The participant saw the desired exertion pattern displayed on the monitor and applied abduction force to the load cell so that their visual force tracker followed the intended pattern (Fig. 2). After each exertion, RPE was collected; followed by a minimum of one MVC trial. Once the participant MVC reached 70% of Pre-MVC levels, and/or RPE reached above 7, or 1-hour passed, the experiment was terminated. Following termination, the participant was asked to rest with their hand/arm in the fixture for 10 minutes while blood flow was continuously measured. After 10 minutes, the participant performed another MVC test. The participant then rested 10 more minutes before a final MVC test.

5.3. Experimental Design

Blood flow and force were simultaneously assessed as participants completed an intermittent finger abduction task to fatigue the FDI muscle. A repeated measures design was used in which each participant completed a preliminary session, and then three subsequent sessions under each experimental condition.

5.3.1. Exertion Levels

The experimental runs consisted of three varying levels of exertion: 20, 30, and 40% MVC. Focus on the lower-medium levels of exertion was important for two reasons; 1) our earlier investigations demonstrated that outcomes of occupationally-relevant fatigue models diverge at lower to medium levels of exertion, and 2) low-medium levels of exertion are prevalent in real-life working conditions (Rashedi & Nussbaum, 2015). Workers cannot perform high MVC tasks consistently over eight hours of work. Most long-term work, then, is at low-medium exertion levels and intermittent over an 8-hour shift. Thus, gaining more information for these task parameters will improve the relevance of the information obtained.

Additionally, literature has shown that there is a significantly wider dispersion of blood flow variation over lower levels of exertion. A study in the influence of exercise on motor unit activation stated that all MUs in the muscle are activated by the time the EL of 50% MVC is reached (Sale, 1987). Other studies have agreed that the pattern and extent of muscle deoxygenation are similar at 60-70% MVC and 100% MVC, implying full occlusion at exertion levels near 60-70% MVC (Humphreys & Lind, 1963; McNeil et al., 2015; Miura et al., 2019). Because of these limits, looking at ELs over 50% may result in the variation of blood flow measurement beginning to plateau. Not only would high ELs be less relevant in terms of application, but results would be less variable at the expense of resolution in the low levels of EL.

Rather than approaching 50% or 60% MVC, 40% was chosen to increase resolution at low EL conditions and limit the number of resources required to complete the fatiguing task. To allow for a representative study in long-term fatigue, fatigue must be developed over several intermittent contractions. Increasing EL decreases the amount of time it will take to achieve muscle failure, and if fatigue happens too quickly, the ability to directly compare fatigue development to the lower ELs can be compromised. 20% MVC was chosen as a low level of fatiguing exertion, as previous work has shown that little fatigue results from work below 20% MVC intensity (Rohmert, 1960, Gersak & Gersak, 2004). Moreover, the extent of time needed to reach a certain level of fatigue by intermittent contractions lower than 20% MVC can be very long. 30% MVC was chosen as a third level to increase resolution and identify curvature in trends.

5.3.2. Work Pattern

Each participant completed three sessions, fatiguing the FDI at one given level of intermittent exertion per session. Fatigue was measured throughout the experimental run as a decrease in MVC force and an increased rating of perceived exertion. Each EL was examined using a similar pattern of intermittent contraction to control as many confounding variables and sources of noise as possible. For all exertion levels, fatigue was developed using a 90 second cycle time (CT), 50% duty cycle (DC), with MVC trials and RPE feedback every 3-6 repetitions (~4.5-9 minutes) to track fatigue level. The exertion task was terminated when MVC reached 70% of the original value when RPE reached above a 7, or 1 hour elapsed.

CT was set to 90 seconds to allow for a full profile of blood flow response both during and following exertion, while also allowing for enough cycles at 40% MVC to detect a distinct pattern. The DC was chosen to be 50% to allow for enough rest for the participant to complete multiple MVC trials before exhaustion and allow for observation of full blood flow profiles during the intermittent rests. MVC trials were designed as single, 3-5 second trials to avoid excessive fatigue. 70% MVC was chosen as the termination threshold to allow enough time to observe fatigue at high EL, while still allowing for the possibility of reaching this fatigue level at 20% MVC within 1 hour.

MVC trials vary in frequency between the EL conditions to introduce approximately the same of MVC trials before fatigue for all conditions (see Figs. 5, 6, & 7).

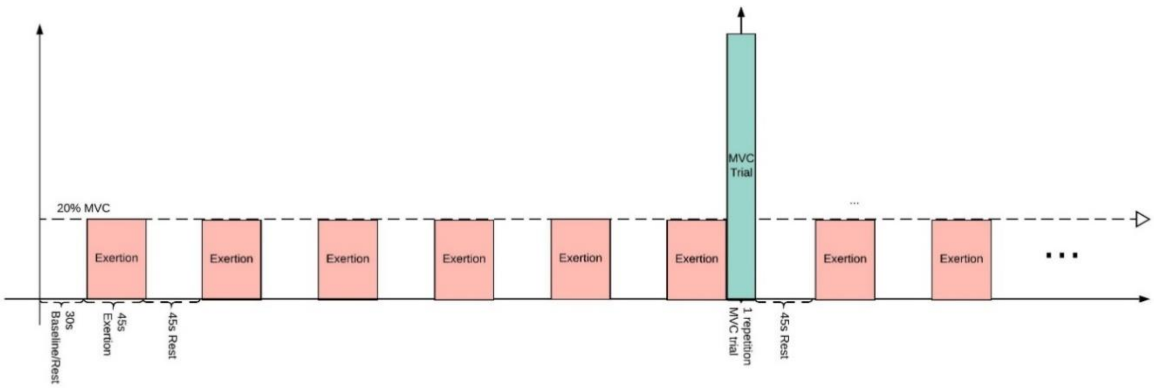

Figure 5: 20% MVC fatiguing pattern with MVC trial following every 6 cycles (9 mins).

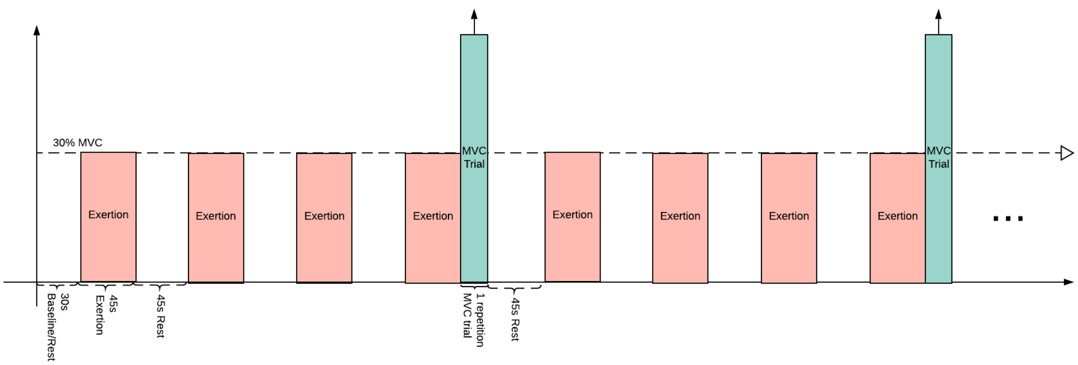

Figure 6: 30% MVC fatiguing pattern with MVC trial following every 4 cycles (6 mins).

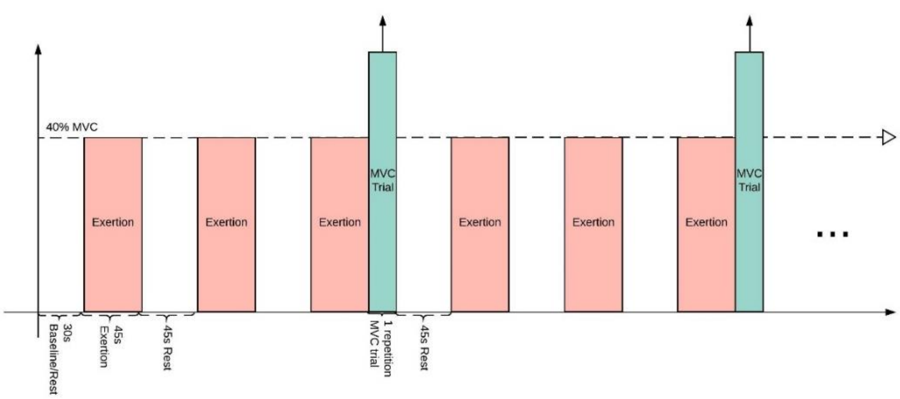

Figure 7: 40% MVC fatiguing pattern with MVC trial following every 3 cycles (4.5 mins).

The MVC trials for 20% EL are the least frequent since it would take more working cycles to elicit the targeted level of fatigue (<70% of initial MVC). In other words, MVC trials, in this case, will most strongly skew this low EL data, as the participant is likely to be able to continue this work for many cycles. Thus, to avoid an excessive number of MVC exertions, a trial is taken after every 6th work period, or, equivalently, every 9 minutes. On the other hand, MVC trials for 40% EL are most frequent. This is because the participant is under the most strenuous exercise conditions and is at the highest risk of hitting muscle failure in between trials. To accurately track and avoid reaching levels of excessive fatigue, MVC trials are taken after every third work period, or, equivalently, every 4.5 minutes.

5.4. Measures and Instruments

To execute the above protocol, force and blood flow data were collected continuously. All other measurements were collected as per Figure 1, with MVC and RPE intermittently tested and collected through experimentation. The two most critical outputs from the experiment were force data and blood flow data. Both blood flow and force data acquisition were controlled using custom LabVIEW programs.

Force data were sampled at a frequency of 1000 Hz, using a 6 degree of the freedom load cell (125 N capacity, Nano25-E, ATI Inc., Apex, NC). The force of interest was in the x-direction, that is, the abduction of the index finger. Force values were reported in terms of %MVC, which is a force measure normalized to the individuals' MVC before the fatiguing exercise.

Blood flow data was measured using a Diffuse Correlation Spectroscopy (DCS) system involving a probe with 785 nm long coherence laser and four-channel photon-counting avalanche photodetector (DL785-120-SO, CrystaLaser, Reno, NV; SPCM-AQ4C, Excelitas, Waltham, MA) (Fig. 8).

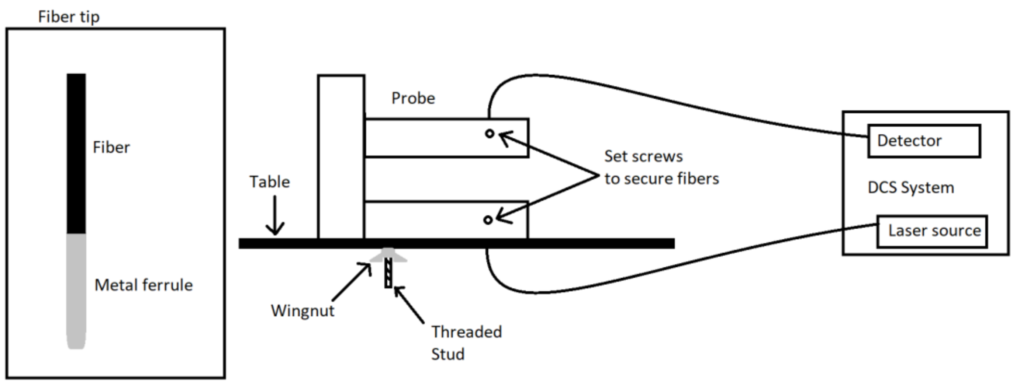

Figure 8: Schematic of the blood flow measurement probe using Diffuse Correlation Spectroscopy.

From detector signals, a normalized intensity autocorrelation curve was calculated from measured speckle light intensity fluctuations using a four-channel hardware correlator board (Flex03OEM, Correlator.com, Bridgewater, NJ). Fluctuation in light intensity is quantified by calculating decay of the light intensity autocorrelation function and is associated with the motion of scatterers in the tissue (i.e. primarily red blood cells) (Durduran et al., 2010). The electric field autocorrelation curve was fit to the semi-infinite slab geometry solution to the correlation diffusion equation, assuming a Brownian flow model. Resulting blood flow index (BFI / αD_B) is the product of the effective diffusion coefficient (D_B) that characterizes red blood cell motion, and alpha (α), which represents the proportion of dynamic to static scatterers BFI values were normalized to the individual's baseline, as measured at the beginning of each session, resulting in a relative blood flow (rBF) value. DCS was the chosen form of blood flow measurement because it, (1) directly measures the movement of red blood cells, (2) can collect real-time, continuous data, and (3) can non-invasively and accurately measure blood flow within microvasculature (Hou et al., 2019).

Force and BF data were synchronized using manual marking in the rBF system and aligning these marks with the force collection. These marks were created at the beginning and end of each exertion (every 45 seconds) to allow for accurate alignment of the data.

Ratings of perceived exertion (RPE) data in the CR-10 Borg scale were also collected following every exertion (Borg, 1982). Muscle capacity was also recorded through an MVC test following every working period.

5.5. Data Analysis

5.5.1. Data Cleaning and Exclusions

For each participant and each session, blood flow data was normalized to the average value of BF observed following initial MVC trials and rest period, and before the first working period exertion. Notably, the blood flow values observed before the initial MVC trials were unstable for most participants. Observations of baseline blood flow following MVC trials and rest showed more consistent readings.

Blood flow data was cleaned to exclude outliers associated with motion artifact, and missing values were filled using linear interpolation. Force data was low pass filtered at 10 Hz and downsampled to 0.5 Hz to align with blood flow data. Following data alignment, all data points were categorized as occurring during a rest period or exertion period, as determined by measured force values. The 4 points that occurred nearest to a transition between rest and exertion, were categorized as transitional points and excluded from both rest and exertion analysis to avoid the effect of motion artifact. Each group of intermittent exertions between MVC trials was indicated as a "working period", beginning at working period 1 and increasing after each MVC trial until the session was terminated.

The data from participant 11 and some data for participants 4 (EL=20%) and 5 (EL=30%) was removed from statistical analysis as rBF values indicated a failure of the DCS system to produce accurate measurements for more than 50% of the data in these sessions. The remaining sessions for participants 4 and 5 were retained.

5.5.2. Analysis Methods

To improve the robustness of the analysis, relative blood flow measurements were fit as average values of rBF over each 45 second period of exertion or rest (X_i values in Fig. 9). For each participant, raw data was converted to a series of average values so that at each exertion level, working period, and cycle, there is one average resting data point, and one average exertion data point.

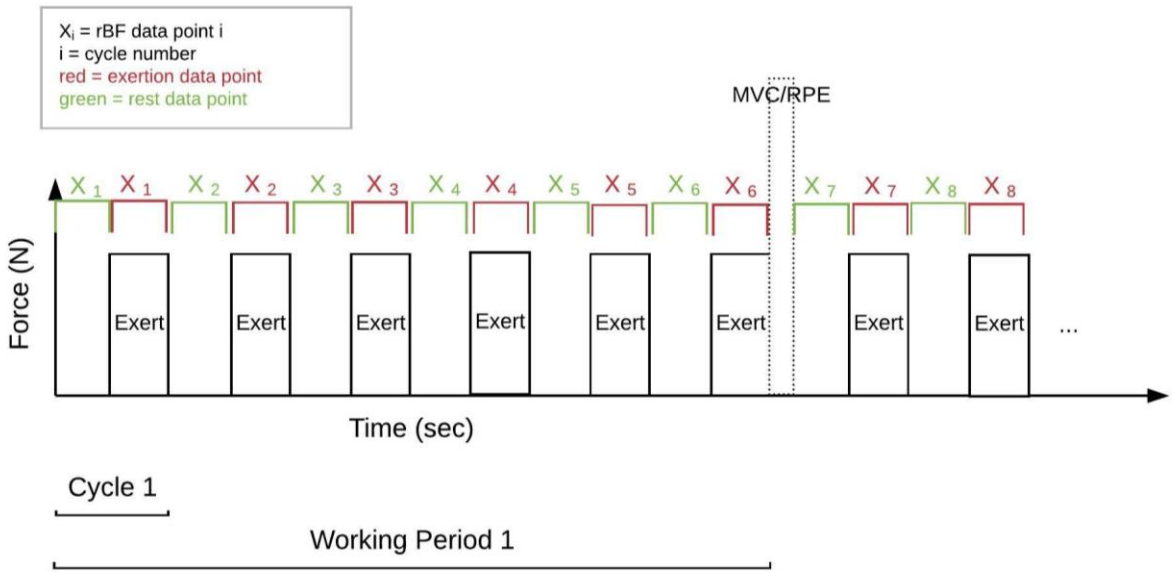

Figure 9: For all participants and exertion levels, sessions were divided into working periods which are bookended by MVC tests. Within each working period were cycles of rest and work, where each cycle is 90 seconds long. Relative blood flow values were averaged over exertion and rest within each cycle.

Analyses were conducted using ANOVA and MANOVA, when appropriate in order to understand how independent variables in the data (Cycle and EL) affect dependent variables, (rBF, MVC, and RPE). Post hoc comparisons were performed using Tukey’s honestly significant difference (Tukey’s HSD) where relevant. Analysis was conducted on periods of intermittent exertion, periods of intermittent rest, and the period of extended rest following each session. All analyses were completed using R, and all statistical conclusions were calculated using a significance value of 0.05.

6. Results

6.1. Characteristics of Blood Flow Response

6.1.1. Response Speed

A significant finding across all participants was nearly instantaneous blood flow response upon initiation of exertion and rest. As shown in figure 10, data resolution indicates that significant changes in BF can be identified within 4 seconds of initiating exertion or rest. This response speed was observed at all levels of exertion, even when accounting for the potential effect of motion artifact and agrees with responses seen in past studies (Hamman et al., 2004).

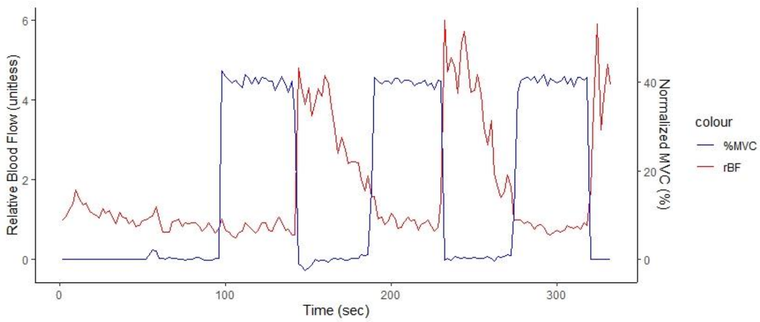

Figure 10: An example of a 40% exertion level blood flow response on the first working period. Blue lines indicate changes in abduction force, while the red lines indicate changes in blood flow.

Though the magnitude of blood flow changed throughout each session, the reflexivity of the blood flow measurement was found to be generally stable within every session, indicating a true biological response (Fig. 11).

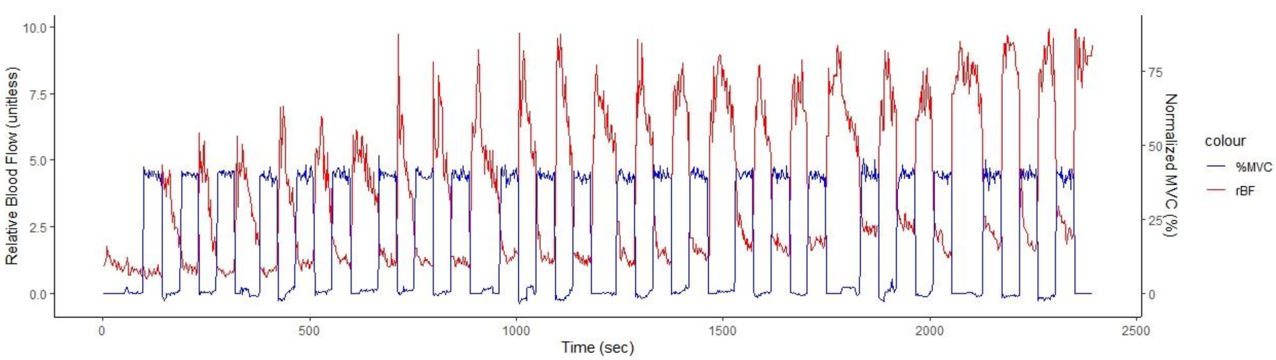

Figure 11: An example of a 40% exertion level blood flow response over all working periods. Slightly longer cycles indicate where <5 seconds of additional time of rest was required to stop the system for an MVC test and then restart the system again.

6.1.2. Response Shape

The shape of the blood flow response occurred in a notable pattern as fatigue increased. At low levels of fatigue, the profile of resting blood flow shows an initial increase and then a gradual decrease over the 45-second rest. In contrast, as fatigue increased, BF tended to remain elevated over the rest period. This is displayed in figures 12 and 13.

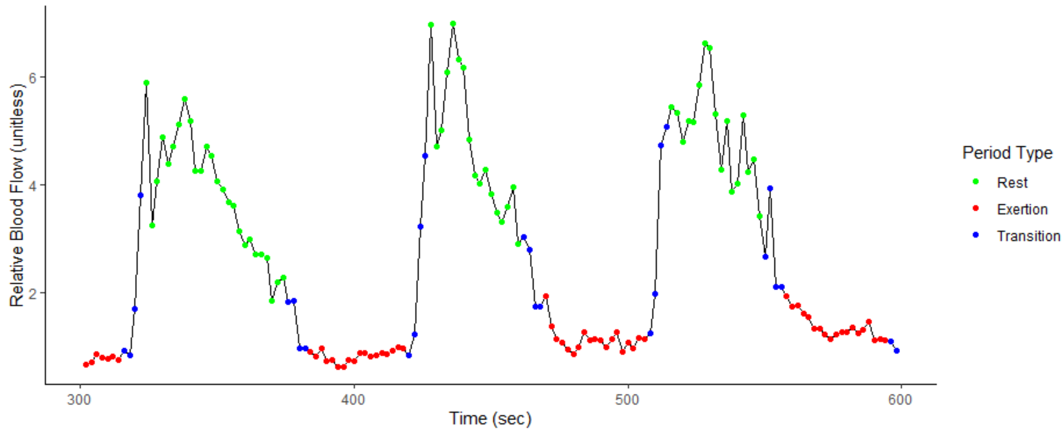

Figure 12: The blood flow profile for participant at an early working period of 40% exertion; representative of blood flow profile at low levels of fatigue.

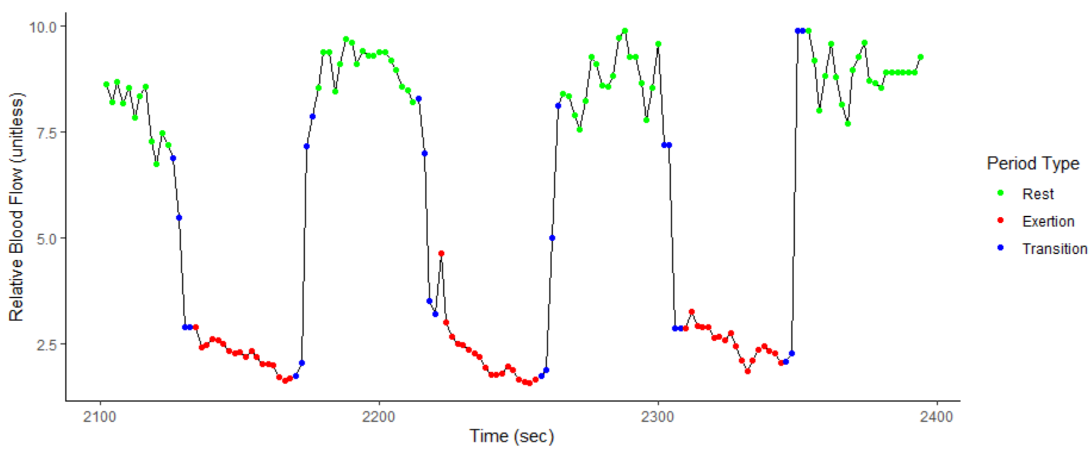

Figure 13: The blood flow profile for the same participant from Fig. 12, at a late working period of 40% exertion level; representative of blood flow profile at higher levels of fatigue.

In addition to noise management, the decision to analyze rBF as the mean value for an exertion or rest cycle was partially to represent these trends in reported rBF values.

6.1.3. Overall Trends

6.1.4. Intermittent Exertion and Rest

Figures 14 and 15 display the general relationships present in the data between exertion level (EL), relative blood flow (rBF), and fatigue (MVC and RPE) during both exertion and rest.

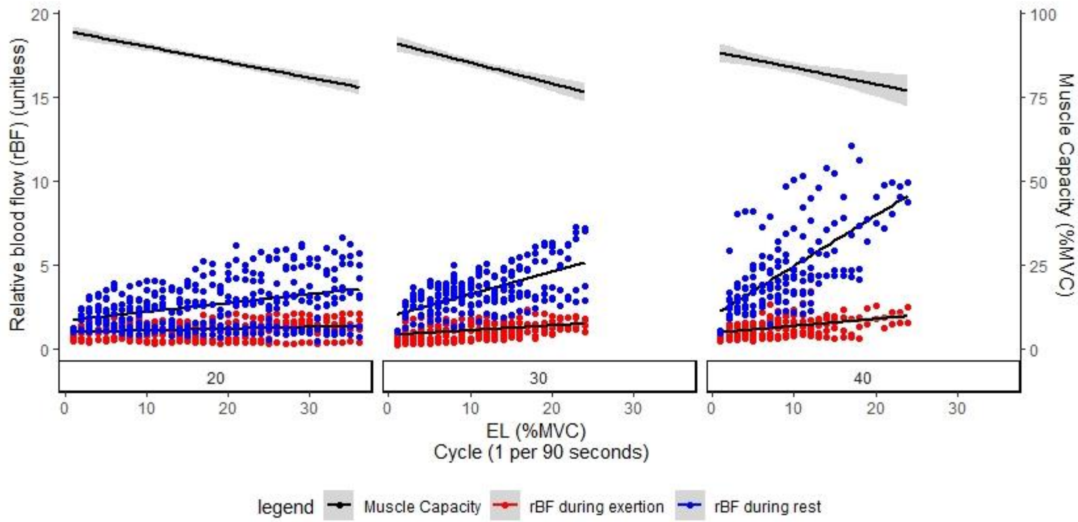

Figure 14: Relative blood flow plotted against cycle. Color indicates rest versus exertion and panels indicate exertion level. Black lines above the BF data are the linear best fits for maximum voluntary contraction values by cycle, with 95% CI.

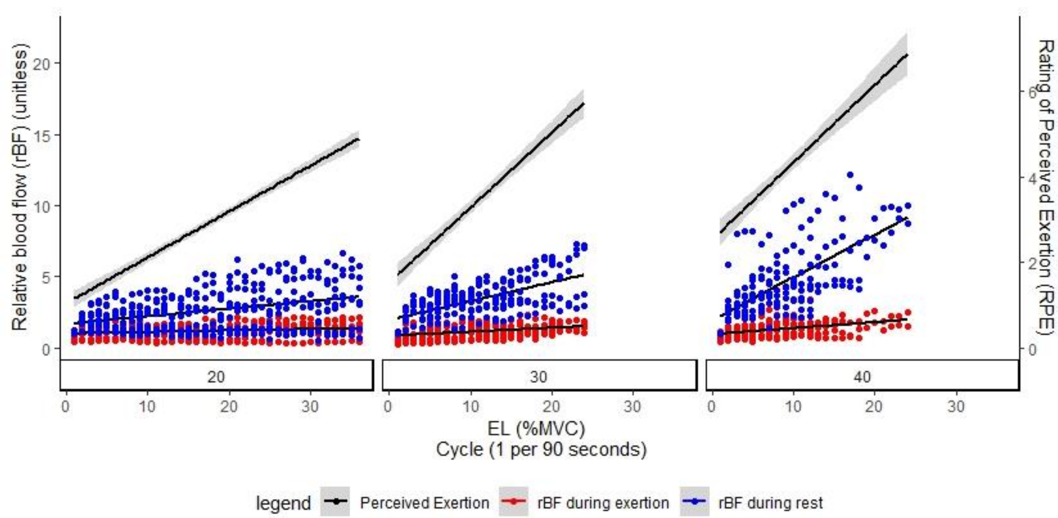

Figure 15: Relative blood flow plotted against cycle. Color indicates rest versus exertion and panels indicate exertion level. Black lines above the BF data are the linear best fits for maximum voluntary contraction values by cycle, with 95% CI.

In Figs.14 and 15, it appears that the spread of rBF is different between ELs. ANOVA was conducted on these three EL groups for both exertion and rest to determine if there are any significant differences in rBF between ELs; Tukey HSD results are shown in the boxplot below, where ELs that share a letter and color are statistically equivalent.

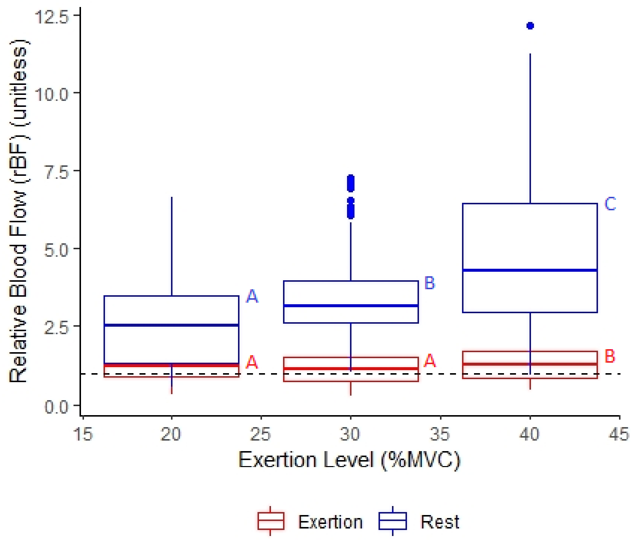

Figure 16: Boxplot of all relative blood flow (rBF) values by exertion level and exeriton versus rest period. Dotted line indicates baseline (rBF=1). Letters indicate statistically similar groupings within rest and exertion using Tukey's HSD (p<0.05).

According to ANOVA, all resting BF is statistically different from exertion blood flow for all levels of exertion. Within rest and exertion, Tukey HSD results are shown in in Fig 16, and indicate that all groups are different excluding 20 and 30% EL rBF during exertion. Blood flow during exertion periods is much lower than that seen during rest periods; the increase in rBF across ELs is also much more prominent in the rest data.

To test if fatigue changes with EL, ANOVA was also conducted on ELs with MVC as a response. Tukey's HSD results for MVC over each exertion level is shown in the table below.

Table 1: Tukey's pairwise comparison results of percent MVC by exertion level.

Pair	Difference	p-value
20-30	-0.02	0.01e-10
20-40	-0.02	0.01e-10
30-40	-0.003	0.24

These results indicate that there is not a statistical difference between fatigue rates at 30% and 40% EL. However, MVC at 20% EL is statistically different from the others.

The significant vertical spread of the points shown in Figs. 14 and 15 is indicative of random effect in the data. Plotting rBF separately for exertion and rest, with regression by participant, this random effect seems to be related to the individual participant (Figs. 17 & 18).

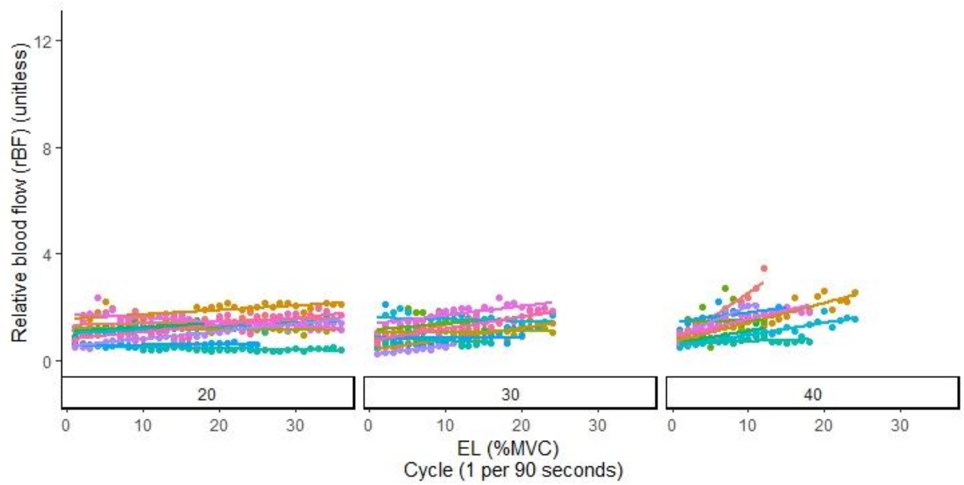

Figure 17: Relative blood flow plotted against cycle, paneled by exertion level, and colored by participant; values during exertion.

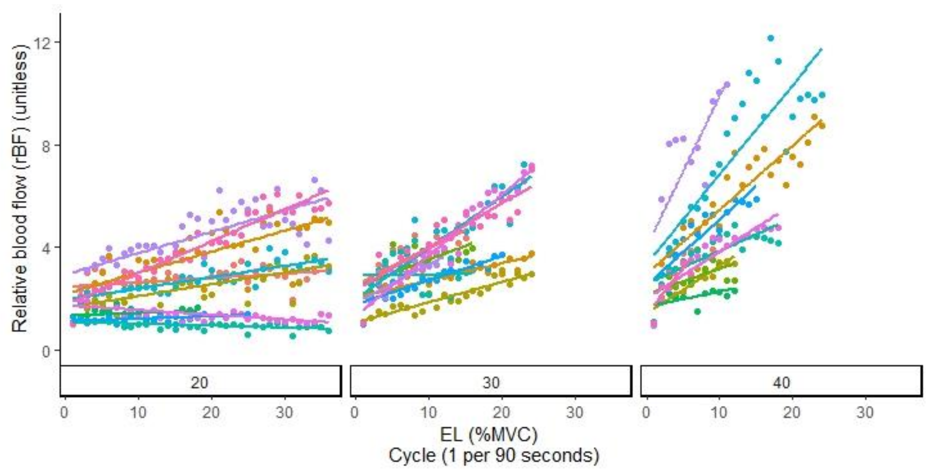

Figure 18: Relative blood flow plotted against cycle, paneled by exertion level, and colored by participant; values during rest.

Looking at the exertion data, we again see the very slight increase in BF across EL. There is no negative slope present across time for any EL or participant. Resting BF in Fig 18 displays similar upward trends at a much larger magnitude. Though there are some differences in slope between participants at each EL, the more significant effect of the participant seems to be the intercept. Though slopes at 20 and 30% may be comparable, slopes at 40% MVC show a distinct increase. Even with the random effect of participants, there is evidence of a difference in trend.

In Figures 14-18 the data also shows a difference between resting and exerting fatigue that appears to increase over cycle. If the data is separated by EL and and ANOVA is conducted on the differences between exertion and rest over cycles, we see that the differences are significantly different across cycle for all ELs. When conducting Tukey's HSD to directly compare levels of cycle within EL, 20%, 30%, and 40% EL result in 0, 39, and 13 significant comparisons between cycles, respectively. These results are shown in Table 2.

Table 2: ANOVA results for the effect of cycle on differences between resting and exerting blood flow; ANOVA separated by exertion level.

Model	20% EL	30% EL	40% EL
P-value	0.04	1.7e-12	1.9e-08
RSE	1.22	0.91	1.99
Qty of significant (p<0.05) cycle pairs (Tukey)	0	39	13

The gradual increase at 20% EL with high random effect explains the lack of significant level comparisons despite an overall significant p-value (RSE 1.22). At 30%, we see a maximum of significant cycles as the increase is more drastic than 20%, and this is combined with the least amount of random error (RSE 0.91). At 40%, we see some significant cycles, mainly between first and last periods due to a drastic increase combined with a similarly large random error (RSE 1.99).

To test if the increase in differences changes depending on EL, ANOVA was also conducted on the differences as a function of EL. The resulting p-value and RSE value were 2.2e-16 and 1.5, respectively.

6.1.5. Extended Rest Period

At the end of each session, participants rested for 20 minutes. MVC and rBF over time are shown in Figure 19.

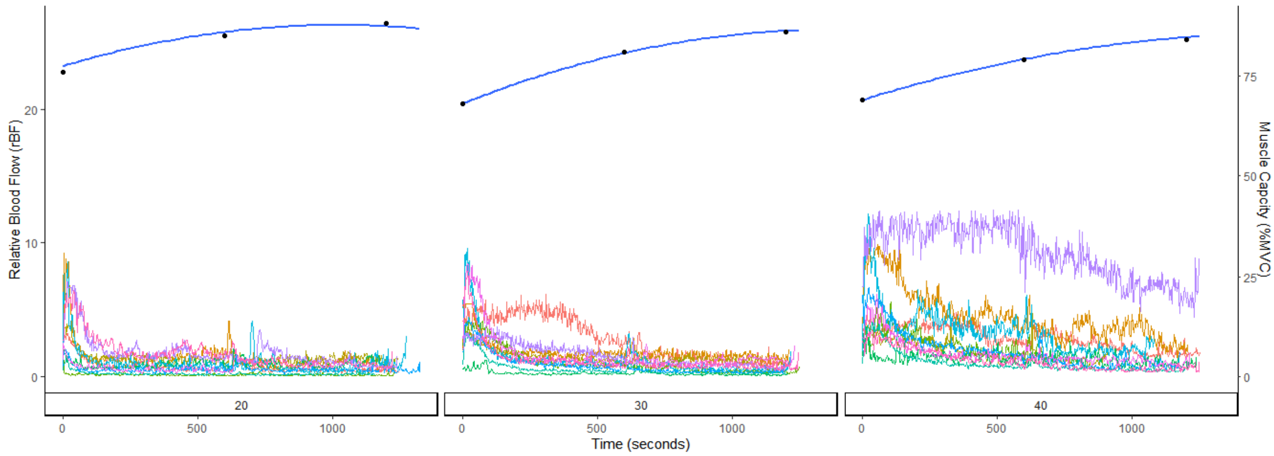

Figure 19: Relative blood flow (below) and MVC (above) plotted over time for the extended rest period following the fatigue session. Blood flow is colored by participant, and MVC is averaged over all participants. Panels indicate exertion levels 20, 30, and 40% MVC from left to right.

The trends in figure 19 show a particular outlier for 40% MVC. This data was retained for analysis because (1) rBF values were consistent with the rBF values observed leading up to the rest, and (2) in this particular session, the participant exhibited particularly high levels of fatigue throughout the entire 20 minute rest (average MVC, average RPE = 66%, 9.0). Thus, these values of rBF may be reasonable.

The rates of MVC recovery were compared based on EL using ANOVA to determine if the amount of capacity a person recovered over these periods was significantly different depending on EL. These rates of recovery were calculated as the straight-line slope between MVC measurements. Two rates were considered, one for the first half of the rest period (first 10 minutes), and one for the second half of the rest period (last 10 minutes). The rate of MVC recovery was not significant for the first or second period of rest based on EL ($p=0.81$, and 0.65 respectively).

Though the rates are not different, the absolute values of MVC were also tested. This was tested by creating MVC~EL models for the initial MVC reading at the beginning of rest, the MVC reading after 10 minutes, and the final MVC reading at 20 minutes. No results show that the MVC values at the beginning, middle, and end of exertion are different based on EL.

Table 3: Tukey's pairwise comparisons on exertion level for MVC values collected throughout rest.

	Pair	Difference	p-value
Initial MVC (t=0)	20-30	-0.08	0.46
	20-40	-0.06	0.56
	30-40	0.01	0.98
Intermediate MVC (t=10 min)	20-30	-0.04	0.79
	20-40	-0.07	0.57
	30-40	-0.02	0.93
Final MVC value (t=20 min)	20-30	-0.03	0.88
	20-40	-0.04	0.72
	30-40	-0.01	0.95

Though overall the effect of EL was not significant for any MVC value, the effect of participants was significant for the first two MVC values (t=0 and t=10 min), but was not significant at t=20 min. This indicates that there are some significant random effects that must be considered.

Blood flow values over time did show some significant differences based on EL. The results of Tukey's comparison tests for each half of the rest period are shown in Fig. 20, below.

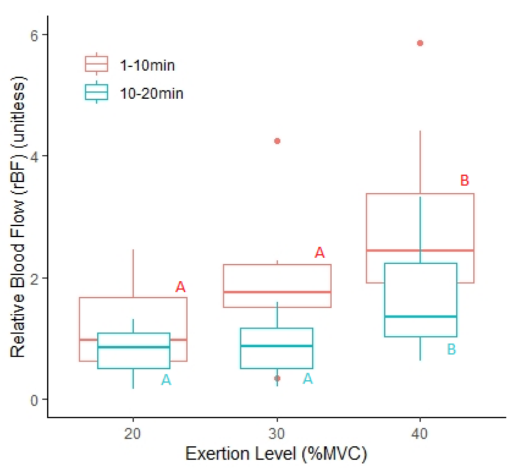

Figure 20: Average relative blood flow values by exertion level. Colors indicate values from the first or second half of the rest period.

6.2. Effect of Exertion Level

Considering these findings, we further investigated the effect of exertion level on blood flow (rBF) and muscle capacity (MVC), considering both dependent variables together in order to better understand their interaction. Before fitting any MANOVA model, boxcox transformations were done on rBF and MVC over time to improve constant variance. Boxcox indicated that transforming rBF to $rBF^{0.5}$, and MVC to $MVC^{3.5}$ for intermittent exertion and rest models would slightly improve variance and, thus, improve the quality of statistical conclusions. For the period of extended rest, Boxcox results indicated that to improve conclusions, rBF would be transformed to ln(rBF) and MVC would be transformed to $MVC^{0.5}$.

6.2.1. Intermittent Exertion and Rest

$$rBF^{0.5} + MVC^{3.5} \sim x_{EL} + x_{Cycle} + x_{EL}x_{Cycle} + \varepsilon \qquad \text{Eq 1.}$$

Results for the MANOVA described in equation 1 are shown in in Tables 4 and 5. Results indicate that EL, Cycle and the interaction between EL and Cycle are significant for rest and exertion.

Table 4: MANOVA on blood flow MVC during exertion periods, using Wilks lambda to calculate F.

	Df	Wilks approx	F	Pr(>F)
EL	1	1.0	7.4	6.9 e-04 ***
Cycle	1	0.8	105.0	< 2.2e-16 ***
EL:Cycle	1	1.0	10.9	2.2e-05 ***

Table 5: MANOVA on blood flow and MVC during rest periods, using Wilks lambda to calculate F.

	Df	Wilks approx	F	Pr(>F)
EL	1	0.8	102.2	< 2.2e-16 ***
Cycle	1	0.7	150.9	< 2.2e-16 ***
EL:Cycle	1	0.9	50.3	< 2.2e-16 ***

Because EL and Cycle are significant, data was segmented by capacity and analyzed across ELs for each capacity level. This allowed for an analysis that considers both rBF and MVC and can reveal any potential interactions between the dependent variables. Blood flow values at each capacity level are shown below, for both exertion and rest (Fig. 21). Within-capacity Tukey comparison results are shown beneath each boxplot, showing the statistical differences between ELs for each condition.

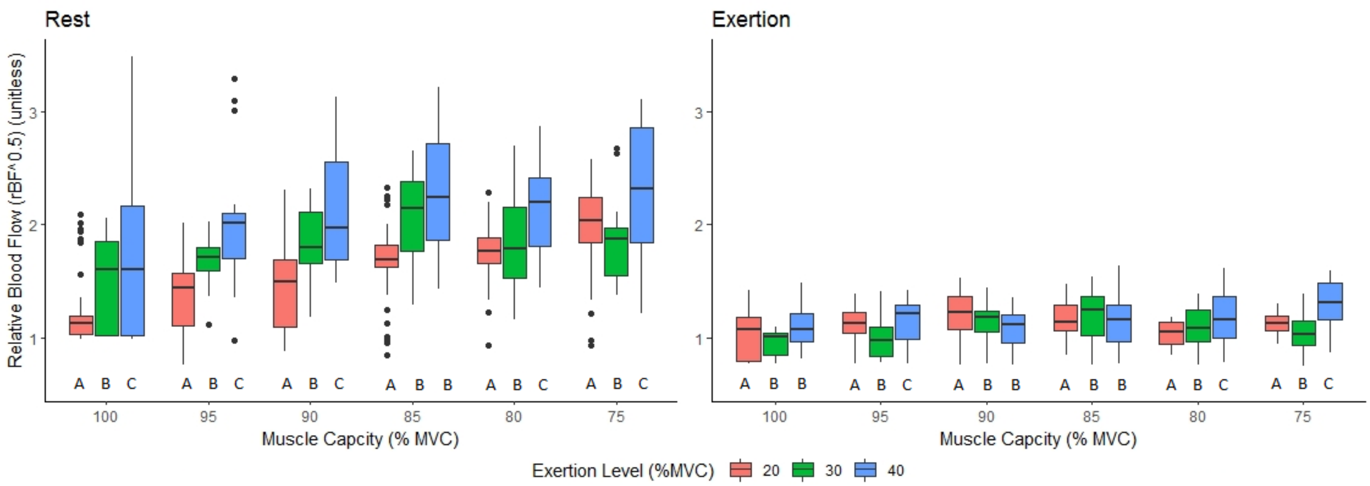

Figure 21: Relative blood flow values (rBF) are plotted against muscle capacity (MVC) for intermittent rest (left) and exertion (right). Within each MVC, rBF is segmented by exertion level (EL). Statistically similar ELs within each MVC are indicated by a similar letter beneath the boxplots (Tukey).

In Fig. 21, we can, again, see the large differences between exertion and rest periods. As capacity decreases, we can see the overall rBF values increase, though this increase is more significant for resting rBF values. For the rest periods, we see that for nearly all MVCs, EL does statistically affect rBF. Excluding one case (75% MVC), average rBF steadily increases with increasing EL. At 75% MVC, BF at 20% EL exceeds that seen at 30%, but not by a large amount. 30% EL rBF does not consistently tend toward 20% or 40% EL, likely because the increment of 10% EL is very small. However, the differences between 20% and 40% MVC are very clear and consistent. Notably, the differences between 20% and 40% MVC get smaller as MVC increases, indicating that the effect of EL may decrease with increasing levels of fatigue. During exertion, ELs are largely statistically different, but the pattern of increasing rBF with increasing EL is only prevalent at higher levels of fatigue (<80% MVC).

6.2.2. Extended Rest Period

In order to conduct a multivariate analysis to assess the potential relationship between the muscle fatigue and blood flow due to the progress of time and changes in EL, MANOVA was used with the following equation.

$$\ln(rBF) + MVC^{0.5} \sim x_{EL} + x_{time} + x_{EL}x_{time} + \varepsilon \qquad \text{Eq. 2}$$

Results for the Eq. 2 MANOVA are displayed in Table 6.

Table 6: MANOVA on blood flow and MVC during the extended rest period, using Wilks lambda to calculate F.

	Df	Wilks approx	F	Pr(>F)
EL	1	0.7	7.65	1.0e-05 ***
Time	1	0.8	10.57	7.3e-05 ***
EL:Time	1	1.0	0.7	0.60

Results for this MANOVA indicate that EL and Cycle are significant, but the interaction is not. This implies that as time goes on, the ELs do not affect the responses differently. Each EL is consistent across time in how it affects the response.

While MANOVA indicates that EL does not affect the responses differently over time, the shapes of the rBF graphs over the rest indicate that this difference may be most relevant at the onset of rest, where the rBF graph shapes most significantly differ between exertion level (Fig. 22).

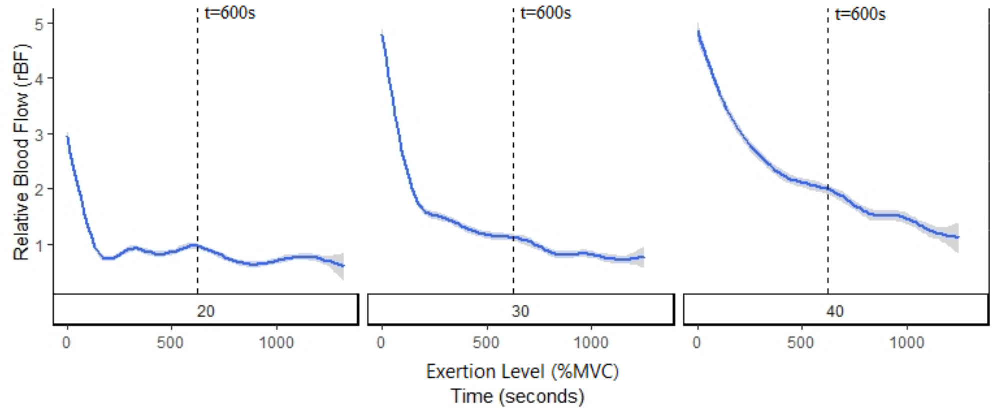

Figure 22: Average blood flow plotted against time and fit using a Loess regression. Vertical lines indicate where the rest period is split in half for analysis. Differences in rBF due to EL appear to decrease as rBF values converge over time.

The rBF values seems to be most affected by EL at the onset of rest, and the impact of EL seems to decrease over time and rBF values converge. To investigate this effect in light of MVC, Figure 23 shows how EL affects rBF for the first 120 seconds of rest (left), versus the last 400 seconds of rest (right). These time segments were chosen to emphasize where EL is hypothesized to have the most and least effect on rBF.

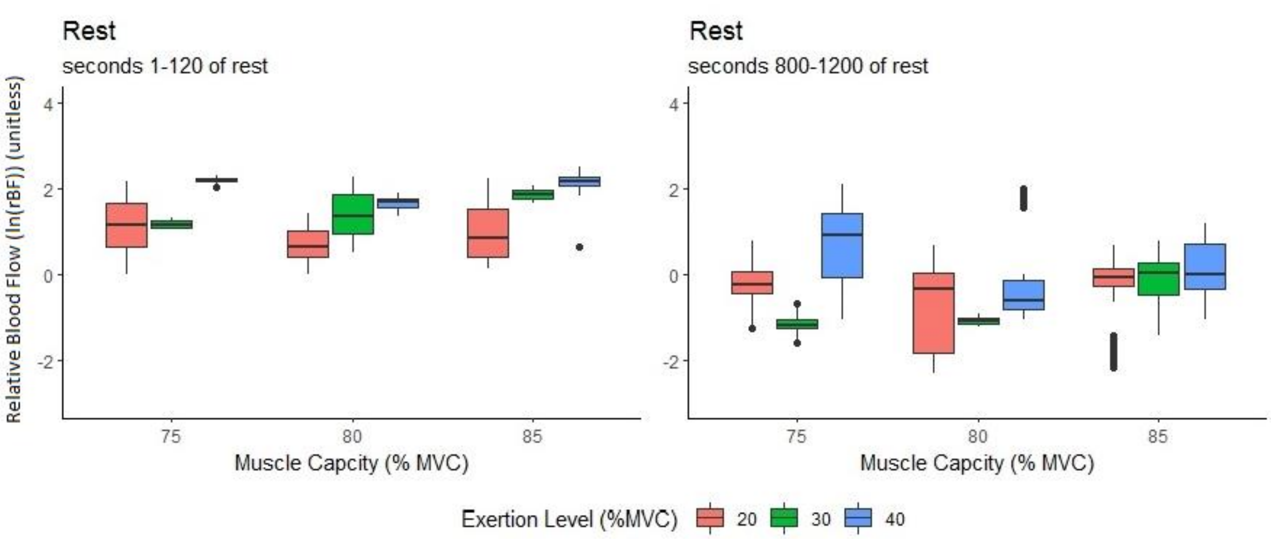

Figure 23: Relative blood flow values (rBF) are plotted against muscle capacity (MVC) for the beginning of the rest period (first 120 seconds, left), and the end of the rest period (last 400 seconds, right). Within each MVC, rBF is segmented by exertion level (EL).

Figure 23 suggests that in the early stages of extended rest, results look very similar to those seen during intermittent rest. EL seems to be positively correlated with rBF at all levels of MVC. Toward the end of the 20-minute rest period, the relationship between EL and rBF looks somewhat random for all levels of MVC. This positive correlation is not seen to the extent that it exists during intermittent rest, or in the first few minutes of extended rest.

7. Discussion

The purpose of this experiment was to characterize the relationship between fatigue and blood flow (BF) during intermittent, submaximal contraction. Understanding how BF and localized muscle fatigue (LMF) are related throughout the exercise, provides insight into the role blood flow plays in the recovery of muscular capacity over time. This relationship was analyzed over varying exertion level (EL) while retaining constant cycle time (CT), duty cycle (DC), and experimental procedure. Variation in EL was chosen to isolate the effects of varying intramuscular pressure and work intensity on rBF and fatigue.

7.1. Physiological Legitimacy of Findings

7.1.1. Blood flow during exertion versus rest

The mean and median of blood flow during exertion was 1.2 times the baseline BF value. In contrast, the mean and median of blood flow levels during rest periods was 3.3 and 3.0, respectively. On average, difference between exerting and resting BF was 2.1, where this difference ranged from ~0 to 11.2. The magnitudes are reasonable, as other studies have reported that the skeletal muscle blood flow can increase in the range of 20 to 50-fold (or potentially more) during maximal exercise, depending on the mass of the muscle and cardiac output (Joyner & Casey, 2015). Given the submaximal nature of this work and the very small mass of the FDI muscle, increases up to 12-fold agree with these values.

The consistent suppression of blood flow during exertion is reasonable, as intramuscular pressure has been found to effect blood flow with exertion levels as low as 5-10% MVC. The continuous increase of blood flow during exertion is supported by other studies which have found blood flow to be unable to be fully occluded until 60-70% MVC contraction (Humphreys & Lind, 1963; McNeil et al., 2015).

In this study, one of the major observations was distinct increase in resting blood flow over the course of a fatiguing exercise. Though a small increase in exertion blood flow was observed, resting blood flow increased at much higher rates. The rate of increase in blood flow was found to be somewhat correlated to a decrease in capacity (cor=-0.26, p-val=3.8e-12). This is expected, as the variables which drive fatigue and those that drive blood flow are also correlated. Force production in the muscle is known to be primarily affected by ATP utilization (Haan & Koudijs, 1994). As discussed in the review above, ATP can be produced either aerobically or anaerobically, and fatigue begins to appear when ATP production fails to match demand in the absence of sufficient oxygen. The beginning of anaerobic ATP production is associated with increased levels of lactate and H^+. The role of BF is primarily the delivery of oxygen and removal of byproducts like Lactate and H^+ to, thus, BF directly impacts resulting fatigue, making the variables highly correlated.

7.1.2. The independent relationship between blood flow and exertion level

Despite these high levels of correlation, this experiment found that over all levels of muscular capacity, from 70%-100% MVC, exertion level affected rBF values. Blood flow was found to increase with increasing exertion level at the same capacity, and the differences between 20% and 40% exertion level blood flow were most prominent. An increase in blood flow that is independent of muscular capacity indicates that exertion intensity has an independent effect on blood flow and MVC during these intermittent rest periods.

The observation of blood flow increasing independently with EL has been observed in past studies. Tension-time index (TTI) was created as a way of defining the total contractile work associated with a task, varying exertion level, and duty cycle. When tasks of identical TTI were compared against blood flow, the exertion level was found to increase BF independently (Richards et al., 2012). A similar study in handgrip exercise came to identical conclusions in a series of experiments varying exertion level and duty cycle (Richards et al., 2010). There is consensus, then, that increases in blood flow have been found to be related to exertion intensity.

One explanation of the EL effect is that BF has been found to respond both as a reflex, and in response to metabolic need. The reflexive increase in BF is in response to physical deformation of receptive fields (mechanoreceptors); the metabolic increase in BF is in response to metabolic stimulants (metaboreceptors). It is popular to equate BF with the energy cost of work, and many studies come to this conclusion. However, because BF responds to mechanoreceptors as well, research suggests that energy cost alone does not drive BF. Rather, muscle fiber recruitment, mostly associated with EL, also plays a part to BF response (Richards et al., 2010). The number of motor units recruited-- directly related to the amount of physical distortion perceived by the system--results in higher levels of BF response. Thus, at the initiation of each rest period, the reflex response.

The reason this effect may have been overlooked in the past is that at high levels of exertion or fatigue, this mechanoreceptor effect is overwhelmed by the effect of metaboreceptors. An example from this study is that, as fatigue increased, the difference between 40% and 20% EL rBF response decreased; this may be due to the metabolic demand increasing to the point that reflexive response is drowned out. The hand-grip study found that increasing EL to maximal or near-maximal contraction also decreased the independent effect of EL on BF (Richards et al., 2012). This may simply be due to the reflexive response reaching a plateau at some EL. At some threshold, (possibly at 60-70% MVC where intramuscular pressure causes full occlusion), differences in EL no longer produce different magnitudes of reflex response (Humphreys & Lind, 1963). Following this logic, the drowning out of the reflex response would also be seen in conditions of long-term rest (i.e., very long cycle time). In this study, the extended rest period exhibited this response. As time went on, the effect of EL became less prominent, as rBF levels began to converge.

This reflex effect on BF may be why, at low levels of exertion, we see that short cycles of intermittent work produce less fatigue than long cycles of intermittent work, even when energy cost is equivalent (Rashedi & Nussbaum, 2016). Since the impact of BF increase is a reduction in fatigue, (by providing O_2 and removing detrimental metabolites), the impact of this reflex is also a reduction in fatigue. The impact of the reflex is maximized under conditions of low EL, where the quanitity of contractions is large (i.e., cycle time is low). So, it follows that conditions of short cycle time and submaximal exertion level slow the rate of fatigue.

7.2. Implications for Fatigue Modelling

In the above review, different types of fatigue models were discussed, and the case was made for the value of parameter-based phenomenological models in the area of ergonomics. The practical application of fatigue modelling benefits from a theoretical design with easily measurable inputs, (preferably related to task condition rather than physiological variable). The needs of practical application are best met in the three-compartment model (Liu et al., 2002; Xia & Frey Law, 2008). The recovery aspect of this model has since been improved to better predict fatigue during low levels of exertion and intermittent exertion (Looft, 2014; Xia, 2014). Our results will be weighed primarily against this model of fatigue and its subsequent improvements.

7.2.1. Total recovery versus active recovery

As previously discussed, the 2008 compartment model by Xia and Frey Law is based on compartmentalizing a pool of motor units into three categories: fatigued, rested, or activated (M_F, M_R, M_A). Movement between these states is defined by equation 3.

Equation 3: Movement between compartments as described by the Xia and Frey Law model.

$$\begin{cases} \dfrac{dM_R}{dt} = -C(t) + R.M_F \\ \dfrac{dM_A}{dt} = C(t) + F.M_A \\ \dfrac{dM_F}{dt} = F.M_A - R.M_F \end{cases}$$

In this model, R is a constant model parameter value that drives the rate of recovery. Rate of recovery is based both on this R value and the size of the M_F compartment (amount of motor units fatigued).

In a 2012 paper by Frey Law, Looft, and Heitsman, the optimal levels of R and F are calculated for a series of different joints and tested over a range of exertion levels/test intensities (10-90% EL) (Frey Law et al., 2012). Working at the joint-level allows normalized fit of R and F to the joint torque, which tends to follow muscle fiber type (i.e., joints with a high number of slow twitch fibers result in lower F and R values than joints with a high number of fast twitch fibers). While this model allowed for good fit at low intensities, where R is more relevant, it was still only appropriate for static exertion.

To adjust the model for intermittent exertion, Looft introduced an additional multiplier (r) to incorporate rest periods (Looft, 2014). This multiplier is only in effect in times of complete rest (EL=0) and increases the R by a factor of r. To obtain optimal values of r, the study employed a similar, joint-specific optimization technique to improve prediction in joints with varying muscle fiber composition. The r parameter decreased prediction error during intermittent contraction by ~100%.

The results of this study support Looft's proposal of an r parameter. Recovery during rest periods was distinctly different than that seen during exertion periods for all ELs ($p<2e-16$). During Looft's model optimization, optimal levels of r for the ankle, knee, grip, and shoulder fell between 11 and 26 (Looft, 2014). This study saw r levels between between 1 and 11. Considering the size of the FDI, these magnitudes may be comparable.

Results of this study also support the correlation between M_F and rate of recovery. This correlation was most extreme in measurements of resting BF. The differences between resting and exertion blood flow were found to be affected by cycle, and, in turn, fatigue level for all ELs (Table 2). Exertion BF showed a possibility of a similar correlation, but the magnitude of cycle's effect was very small when compared to resting BF (Figure 16). If this correlation is truly significant during exertion, this follows past findings that R is best fit very small (<.001), and r is best fit between 1 and 40.

7.2.2. Implications of the exertion level effect on blood flow

In contrast to current modeling of the r parameter, when the cost of work is stable, this study did not find r to be consistent across all exertion levels. For MVC values between 75 and 100% MVC, exertion level was found to consistently increase rBF, and, thus, r, during rest. This is likely attributed to the BF response to mechanoreceptors, which is highly correlated with intensity of exercise (i.e., exertion level). We also saw that as rest continued, there is evidence that reflexive blood flow response is only relevant for a limited amount of time; this effect becomes diluted over rest time by the BF response to metaboreceptors (see Fig. 22). Thus, the effect of exertion level on BF is likely relative to the DC and CT, or, alternately the length of the rest period. If we observe the effect of reflex to become diluted over time, it is also logical to assume this reflex will become more diluted over increasing MVC as well. As fatigue increases the metabolic demand of the muscle, this demand may begin to far exceed the effect of reflex, to the point that the impact becomes very low. These findings imply that the r parameter may be better represented as a function of EL, where r is elevated according to EL for a short period time after initiating rest.

Xia's model introduced in 2014 proposed R as a function of EL, however, the effect of this change was negligible for models of both static and intermittent exertion. In this case, R was given a linear relationship with EL for MVC values from 10-50% MVC (Xia, 2014). This parameter change affected R (recovery rate during exertion and rest), rather than r (recovery rate multiplier in effect *only* during rest).

In this study, we found that the effect of exertion level was not the same during rest and recovery (Fig. 21). Thus, in order to better represent the changes in BF we observed, an additional rest multipler (r) should be added to the model, and this r should be a function of EL. Making R a function of EL as well may be additionally beneficial, but the results from this study are not conclusive on the effect of EL during exertion. Based on our observations over ELs of 20-40%, if EL does have an effect on exertion BF, it is at least not to the same magnitude of the effect of EL on BF during rest.

7.3. Limitations and Future Work

The statistical results of this study were limited by error due to individual differences in rBF measurement. These inconsistencies were caused by a series of outside factors that I would not consider true difference: (1) Lack of blood flow in the FDI before exertion, and (2) insufficient baseline collection time. There was some difficulty in getting true measurements of baseline rBF before MVC trials. We hypothesize this is due to poor circulation in the hand, and levels of blood flow so low that DCS could not read correctly. This issue was partially resolved by collecting baseline values following MVC trials and before exertion for all participants. As a result, the baseline values collected were not true baselines. Additionally, the baselines that were collected were still jittery for some participants whose rBF values still seemed to be affected by initially low levels of BF.

These individual errors could be minimized by extending the time baseline values are collected. The issue of errors could potentially avoided by choosing a larger muscle in which to conduct BF measurements.

Statistical power was limited by the number of participants included in the study. In this case, we included data for 11 participants. However, considering the individual error present in this data, more statistical power could improve statistical analysis.

Additionally, termination criteria made some results at 20% MVC less statistically sound. Rather than terminating the session at an hour, the time should have been extended to allow more participants to fully fatigue within the timeframe to obtain more data points at high levels of fatigue for this EL.

We are also aware that using the FDI may limit the relevance of these results to larger muscles. Increases in blood flow were smaller than some other studies have found (12 fold increase as opposed to 20 fold increase), and we hypothesize this could be the result of the FDIs small size and distance from the heart.

Another limitation is the effect of central fatigue in our intermittent MVC tests. Though procedures were in place to minimize central fatigue effects, this must be considered when interpreting results. This could be avoided by using electrical stimulation.

Considering that this data was collected under only ELs of 20, 30, and 40% MVC, it may be beneficial to continue the study with additional levels of MVC. Additional data would confirm our trends, and more levels of EL could improve our understanding of the sensitivity of the EL effect. It would also be beneficial to conduct similar experimentation in other muscle groups to determine if these behaviors are still observed, and how they may vary in magnitude. It also may be helpful to conduct a similar experiment allowing fatigue to reach lower rates (below 70% EL). This could provide critical information in understanding if the behaviors we observed here are true even at exceptionally low levels of fatigue.

Finally, it would be valuable to consider the effects of temperature and vibration on these results, as this study did not address or control these conditions and both are known to affect BF (Egan et al., 1996; Song et al., 1989). Research considering these factors would be necessary for application of these results to a dynamic environment like the workplace.

8. Conclusion

This study aimed to observe and understand the relationship between BF and fatigue during intermittent contraction under various conditions of exercise intensity (20, 30, and 40% EL). Results indicated that rBF, (especially resting rBF), was highly correlated with fatigue, statistically increasing over the course of intermittent contraction for all ELs. We also found that at the same level of fatigue, EL was found to increase rBF independently. This increase is likely attributed to the reflexive BF response that is correlated to exertion level (EL). Over time, we found that this relationship between EL and BF begins to lessen in its significance, indicating that the impact of this response is time limited and rBF values converge over time.

Our observations of rBF during intermittent exertion have provided a unique, data-driven perspective from which to analyze the quality of recovery modelling in current parameter-based fatigue models. Large increases in rBF during total rest support the implementation of the additional r parameter proposed by Looft (Looft, 2014). Additionally, the independent influence of EL on BF leads us to believe that some portion of BF increase during rest is the result of the reflexive BF response, making this r parameter a function of EL with a time limit on its effect.

The results of this study are supported by separate physiological findings in the areas of BF and fatigue study. Hand grip studies show that BF increases with EL in situations with the same total energy cost of work; a cycle time study found that short exertion periods slow fatigue (Richard et al., 2012, Rashedi & Nussbaum, 2016). Both of these findings, though from different perspectives, point to the same phenomenon: the impact of the reflex response of BF. Various findings come together in this study in a new way, as rBF and fatigue are observed together. This intersection of physiological study and fatigue study has allowed for a better understanding of the recovery. The continued testing and validation of these findings will be important in improving fatigue models to better represent the recovery process.

9. References

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